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Exogenous Control of the Estrous Cycle in the Mare

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The control of estrus, and more importantly ovulation, may be desirable in a breeding program to service an animal at a predetermined time, to synchronize ovulation in a group of mares, or to spread ovulations over a prolonged period of time according to the various needs of managing the breeding animals. Ideally, the goal would be to control ovulation with enough precision that breeding could be done without the necessity of estrus detection.¹ Three methods of control (or combination thereof) can be used: 1) induction of ovulation during estrus, 2) prolongation of the luteal phase by administration of a progestin, and 3) termination of the luteal phase by administration of Prostaglandin F_{2a} (PGF_{2a}) or one of its analogues. A point to be remembered is that in order to allow any useful control over ovulation time, mares must be either cyclic or so near the first ovulation of the season as to be considered cyclic.^{2,3} It also should be kept in mind that all of the following methods and techniques should be used in conjunction with a good palpation and teasing program.

INDUCTION OF OVULATION

Ovulation induction techniques are widely used in the equine industry due to the long and variable length of estrus. This is intertwined with the highly variable interval from onset of estrus to ovulation. Inducing ovulation shows benefits in improving breeding efficiency in that the number of breedings can be limited per conception. The advantages of conserving a heavily used stallion and decreasing the number of chances of bacterial contamination and injury are easily seen.

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Three types of hormonal preparations are available for induction of ovulation. These are human chorionic gonadotrophin (HCG),^a anterior pituitary extracts, and gonadotrophic releasing hormones (GnRH).

The hormone HCG has predominantly luteinizing hormone (LH) activity. The dosage recommended varies from 1500–3000 IU, and when administered IM gives consistent results.^{4,5,6} A study done by Russian workers has shown a distinct reduction in conception rates post-treatment when using higher dosages than 3000 IU.⁷ The ability of HCG to be antigenic has the potential to cause an immune reaction. Some controversy has existed over the capability of anti-HCG antibodies to cause neutralization of the HCG and ovulatory refractoriness.^{8,9} A recent study¹⁰ has shown a significant antibody titer can be produced following repeated injections over a breeding season but that no ovulatory refractoriness was noted. Anaphylactic reactions are possible but are reported to be rare.⁴ Unused portions of the HCG may be refrigerated or frozen but should be used within 30 days or discarded.

Anterior pituitary extracts are also being used in ovulation induction. These products are isolated from the pituitaries of horses or other species. Pituitary extracts give erratic results compared to HCG in the horse, and have the disadvantage of required freezing of the unused portion to maintain potency.^{4,11} The pituitary extracts do have the ability to induce follicular growth and multiple ovulations during the ovulatory season.¹ The ability of pituitary extracts to cause superovulation may bring increased use as embryo transfer techniques are perfected in the mare.¹²

Finally, the gonadotrophic releasing hormone (GnRH) is being used in ovulation induction.

^aChorisol T. M., Burns-Biotec, Omaha, NE 68127.

GnRH causes release of endogenous LH from the anterior pituitary and appears to be as efficacious as HCG but without the problems with antigenicity. Daily administration of 2 mg beginning on the second day of estrus shortens the duration of estrus and time interval before ovulation significantly.¹⁴ Lengths of the estrus period averaged 11.8 ± 2.1 days in control and 6.9 ± 0.9 days in treated mares. In the group of treated mares, 67% ovulated within 24 hours of GnRH treatment. As of this time, however, GnRH might often be cost prohibitive since a 2 mg dose now costs about \$140.00.

Candidates for induction of ovulation fall into two categories.⁴ First are those mares bred during the seasonal ovulatory period at the optimal time of their estrous cycle but fail to ovulate within 48 hours (of insemination). These mares are clinically normal but may have variable estrus lengths due to individual idiosyncrasies. Management errors are a factor due to poor teasing methods and interpretation. These mares have a history of annual foaling but need multiple breedings per conception. The second group of mares are those which are bred during the transitional phase of their cycle, especially early in the year. These have a history of being barren mares with which attempts are made at an early conception. These transitional mares often show strong signs of estrus, but insufficient LH release from the pituitary impedes ovulation.

The mare should be given a complete exam before undertaking induction of ovulation.⁴ Each mare should meet the following criteria: 1) There should be a palpable follicle, usually 30–80 mm in diameter. 2) The uterine horns should be symmetrical and have an edematous consistency along with the borders of the cervix being short and indistinct due to relaxation. A negative culture and biopsy should be obtained before any breeding attempts when uterine infection is a potential problem, or when the history indicates their use.

Before use of HCG to induce ovulation, careful consideration must be given to all present follicles. The extra LH stimulation may result in multiple ovulations and in increased chance of twinning.⁵ Alternatives are available when faced with multiple follicles.⁴ If there is no hurry to get the mare bred, it would be best to wait until only one mature follicle is present. Some mares can have a "split" ovulation in which one follicle ovulates several hours prior to the other. In this case breeding should be

attempted 12 hours after the first ovulation. This will hopefully allow the first ovum to degenerate while the second is still viable. The other option is to go ahead and breed after ovulation induction since clinical ovulations exceed the actual number of twin pregnancies even though both follicles may rupture simultaneously. Mares which are covered in spite of having multiple ovulations should be checked at 30 days of gestation and proceed to abort the mare if twin fetuses are present.

PROGESTOGEN TREATMENT

The use of progestins as synchronizing agents has been found to be effective in the mare. Unlike some other species, conception rates are not reduced. Treatment with progesterone-like compounds has the advantage of not being affected by the stage of cycle at the onset of treatment as in prostaglandin therapy.¹⁵

Several regimens have been used to control estrus. The most common utilizes a progestogen alone via daily injections for 18 or 19 days.¹⁶ Estrus will occur several days after withdrawal of progesterone. Ovulation can further be synchronized by administration of HCG six days post-treatment.¹ Loy et al.¹⁷ has reported the use of daily injections of 150 mg progesterone and 10 mg estradiol-17B for 10 days along with prostaglandin on the last day of steroid treatment resulting in synchronization of estrus and ovulation in normally cycling mares. More variability again occurs when used during the transition period unless the mares have been adequately stimulated by an artificially increased photoperiod prior to beginning of treatment.¹⁶

An oral progestin, altrenogest,^b has been evaluated in normally cycling mares.¹⁸ A dosage of 0.044 mg/kg suspended in neobee oil appeared to provide the most consistent response and is therefore the recommended dose for broodmares. This dosage is administered once daily for 15 days. The results with this dosage were an interval to estrus of 5.0 ± 2.4 days and an interval to ovulation of 10.2 ± 3.6 days. Conclusions from several studies have shown altrenogest to be an effective tool for minimizing the need for estrus detection and for synchronization of estrus in normally cycling mares.¹⁵ Mares in estrus at the onset of

^bRegumate, American Hoechst Corp., Somerville, NJ 08876.

treatment will cease to exhibit estrus within 2–3 days and will continue to be in quiescence for the duration of treatment. Other products such as norgestomet implants have been used with similar results.

The transition period in the early part of the breeding season is quite often represented by irregular estrus periods. Disruption of this irregularity can be accomplished with intramuscular treatments with 100 mg per day of progesterone in oil for seven days.¹⁹ Van Niekerk et al.²⁰ reported that behavioral estrus was blocked within two days following treatment initiation and that most mares were in an ovulatory estrus within 3 days after the last treatment. Mares not in estrus but with active ovaries responded similarly while those without abundant follicular activity gave poor results.

More recent work has been done using altrenogest to assist transitional mares in establishing normal cycles.^{21,22} In one study where 18 mares which had not exhibited a normal estrous cycle were treated with altrenogest for 12 days, the duration of post-treatment estrus, interval from the end of treatment to ovulation, and interval from the first day of estrus to ovulation were shorter for treated mares than for control mares.³ It was also noted that none of the treated mares experienced split estrual periods, whereas 6 of 9 control mares did.

Several field trials were also done on the use of altrenogest using 440 broodmares at 17 different locations.²³ Results of these field trials have shown altrenogest to be ineffective during the early transition period, but did show shorter post-treatment estrus when used during the late transition period (7.7 days for treated mares vs. 12.1 days for controls). The interval to conception was also less ($P < .5$) for treated mares than control mares (28 days vs. 41 days for controls). These results give further evidence of the ability of altrenogest to both suppress estrus as well as assist mares in normalizing their estrous cycles.

Progestogens are often used for suppression of estrus in mares used for racing, showing or other events. Daily IM injections of 50 mg progesterone in oil beginning prior to the onset of estrus prevents estrus behavior but not ovulation, while 100 mg per day of progesterone is needed to block estrus in a normal, cycling mare if she is in estrus at the start of treatment. The dosage of 50 to 100 mg per day is adequate when the mare is showing estrus during the transitional or anovulatory season.¹⁹ Studies

have also been done using altrenogest for suppression of estrus.¹⁵ A dosage of 0.44 mg/kg daily proved to be effective and safe for extended periods and did not affect subsequent fertility.

PROSTAGLANDIN-INDUCED LUTEOLYSIS

Prostaglandin F_{2a} along with a variety of analogues have shown to be effective luteolytic agents in the mare. The prostaglandins have become valuable therapeutic tools to the equine practitioner as luteolytic agents, both in terminating diestrus and in inducing an early abortion. Indications for the use of prostaglandins for inducing luteolysis include interrupting prolonged diestrus due to a spontaneous persistent corpus luteum (CL), interrupting prolonged diestrus when diestrus prevents normal return to estrus, changing the distribution of estrus in groups of mares booked for breeding to the same stallion to avoid overbreeding, shortening the interovulatory interval when breeding is passed or missed, shortening the interovulatory interval when diagnostic or therapeutic procedures require cervical relaxation, synchronizing estrus in donor and recipient mares in preparation for embryo transfer, terminating pregnancy at up to 38 days of gestation, treatment of mismating, and treatment of those cases of pyometra in which a CL persists.⁵

Prolonged diestrus is a common cyclic abnormality which must be recognized and dealt with. It is due to persistence of a CL and is seen as failure to return to estrus on schedule. Persistent CL may occur spontaneously, in association with pyometra or endometrial degeneration, and possibly along with lactation.²⁵ The increased life span of the CL is due to lack of normal luteolysis. Causes of this failure may be due to lack of prostaglandin (PG), or the presence of antagonistic endocrine substances at the time of PG release. Spontaneous persistence of the CL may last up to 90 days.

Persistence of the CL may also be a result of uterine changes or pathology that blocks PG release.²⁵ Pyometra and endometrial degeneration are the best examples. Pyometra usually becomes a problem only when the cervix is closed and fluid persists in the uterine lumen. Both syndromes inhibit release of PG.

Prolonged diestrus due to early embryonic death after the formation of endometrial cups at day 38 should also be mentioned. The endo-

metrial cups produce pregnant mare serum gonadotropin (PMSG) which apparently maintains luteal function. It isn't clear whether PMSG prevents luteolysis or induces formation of new CLs but PMSG is now thought to have a luteotrophic role.²⁵ PG luteolysis does not work as a treatment for prolonged diestrus of this etiology. Mares will usually not return to estrus until 100 to 120 days, when the PMSG production diminishes. No therapeutic regimen is available in these cases.

As mentioned before, it is often desirable to shorten the interovulatory period in a breeding program via PG luteolysis since the distribution of intervals from treatment to ovulation is quite broad. The average time that can be saved by PG given during diestrus is 1 week.¹⁶ More time can be saved by incorporating HCG which is usually recommended at 6 days following PG treatment.¹

In using prostaglandins, it must be understood that a mature CL must be present in order for luteolysis to occur. This usually translates to at least 4 days post-ovulation before the CL is mature and functional and susceptible to PG luteolysis.

Mares are notoriously unpredictable in their response to prostaglandin-induced luteolysis.⁵ The most important factor which controls this is the follicular status of the ovary at the time of drug administration.²⁶ In one study, mares which had large follicles at the time of treatment showed the most variability in response. With follicles greater than 40 mm in diameter, 33% of these follicles regressed and a new follicle ovulated later. In the remainder of the mares, the large follicle ovulated in shorter than normal intervals of time following treatment. Some mares ovulated 24–72 hours post-treatment while showing minimal signs of estrus.²⁷ Less variability occurs with smaller follicles with the average time from treatment to ovulation being six days.⁵ If large follicles are present, daily teasing and palpation to identify estrus and impending ovulation needs to be done following prostaglandin treatment.

Other variations in response to prostaglandin treatment include partial and complete failure of luteolysis. Results of a study in which a prostaglandin analogue was administered in the presence of a six-day-old CL showed only 65% of the mares responded with complete luteolysis while incomplete luteolysis (where progesterone failed to drop to levels which allow estrus) occurred 26% of the time.²⁸ Recovery of

the CL following incomplete luteolysis occurred 6% of the time while no luteolysis occurred 3% of the time.

There are three commercially available prostaglandin products that are approved for equine reproductive work. A natural PGF_{2a} compound, dinoprost trimethamine,^c is given at a dosage of 10 mg IM. Prostalene^d and fluprostenol^e are analogues which are given at dosages of 2 mg SC and 250 ug IM respectively. A higher number of positive luteolytic responses are seen when two doses are administered on subsequent days.²⁵

Following dinoprost administration, some degree of sweating is almost always observed within 15–20 minutes of treatment.²⁵ This can occasionally be profuse and persistent. Signs of mild colic or abdominal discomfort may also appear but last a short time. A posterior ataxia can also rarely be seen. The PG analogues have few observable side effects and are chosen more often to waylay potential client apprehension than comparative effectiveness of the drugs.

It is important for the reader to understand that many of the methods of estrous cycle control which have been discussed were done on an experimental basis and are not ready to be widely implemented. The use of HCG and PG has been well documented and shown to be quite safe as long as the appropriate dosage and route of administration are followed. GnRH is not approved for use in the equine, but altrenogest recently received clearance and is available commercially. A great deal of work is now being done in these areas and much more will need to be done in the future.

^cProstin, The Upjohn Co., Kalamazoo, MI 49001

^dSynchrocept, Diamond Labs, Inc., Des Moines, IA 50303

^eEquimate, Haver-Lockhart Labs, Shawnee, KS 66201

REFERENCES

1. Ginther, O.J.: *Reproductive Biology of the Mare: Basic and Applied Aspects*, Ann Arbor, MI, McNaughton and Gunn, 1979.
2. Palmer, E.: Reproductive management of mares without detection of oestrus. *J. Reprod. Fert., Suppl.*, 27:263, 1979.
3. Squires, E.L., Stevens, W.B., McGlothlin, D.E. and Pickett, B.W.: Effect of an oral progestin on the estrous cycle and fertility of mares. *J. Anim. Sci.*, 49:729, 1977.

4. Hopkins, S.M.: Ovulation induction. In: *Current Therapy in Equine Medicine*. Edited by N.E. Robinson, W.B. Saunders Co., 1983, pp. 402-403.
5. Asbury, A.C.: The reproductive system. In: *Equine Medicine and Surgery*, 3rd Edition, Vol. 2. Edited by R.A. Mansmann and E.S. McAllister, American Veterinary Publications, Inc., 1982.
6. McGee, W.: Theriogenology and the equine—part I. The broodmare. *J. Soc. Therio.*, vol. 8, 1978.
7. Shilova, A.V., Platov, E.M., and Lebedev, S.G.: The use of human chorionic gonadotrophin for ovulation date regulations in mares. *Proc. Inter. Cong. Anim. Reprod. and Artif. Insem.* 3:204-207, 1976.
8. Loy, R.G., and Hughes, J.P.: The effects of human chorionic gonadotrophin on ovulation, length of estrus and fertility in the mare. *Cornell Vet.* 56:41-50, 1966.
9. Sullivan, J.J., Parker, W.G., and Larson, L.L.: Duration of estrus and ovulation time in nonlactating mares given HCG during three successive estrous periods. *JAVMA* 163:885-898.
10. Roser, J.F., Kiefer, B.L., Evans, J. W., Neely, D.P., and Pacheco, C.A.: The development of antibodies to human chorionic gonadotrophin following its repeated injection in the cyclic mare. *J. Reprod. Fertil, Suppl.*, 27:173, 1979.
11. Lapin, D.R., and Ginther, O.J.: Induction of ovulation and multiple ovulations in seasonally anovulatory and ovulatory mares with an equine pituitary extract. *J. Anim. Sci.* 44:834, 1977.
12. Douglas, R.H.: Review of induction of superovulation and embryo transfer in the equine. *Theriogenology* 11:33, 1979.
13. Irvine, D.S., Downey, B.R., Parker, W.G. and Sullivan, J.J.: Duration of oestrus and time of ovulation in mares treated with synthetic GnRH (AY-24,031). *J. Reprod. Fert.*, Suppl. 23:279, 1975.
14. Roberts, S.J.: Gestation and pregnancy diagnosis in the mare. In Morrow, D.A. (ed.): *Current Therapy in Theriogenology*. Philadelphia, W.B. Saunders Co., 1980, pp. 736-746.
15. Squires, E.L., Shideler, R.K., Voss, J.L., and Webel, S.K.: Clinical applications of progestins in mares. *Comp. on Cont. Educ. for the Pract. Veterin.* 5:S16, 1983.
16. Loy, R.G.: Control of ovulation. In: *Current Therapy in Equine Medicine*. Edited by Robinson, N.E., W.B. Saunders Co., 1983, pp. 404-405.
17. Loy, R.G., Penstein, R., O'Cauna, D., and Douglas, R.H.: Control of ovulation in cycling mares with ovarian steroids and prostaglandin. *Theriogenology* 15:191-200, 1981.
18. Squires, E.L., Webel, S.K., Shideler, R.K. and Voss, J.L.: A review on the use of altrenogest for the broodmare. *Proc. 27th Am. Assoc. Eq. Pract.*: 221, 1982.
19. Hawkins, D.L.: Progesterone therapy. In: *Current Therapy in Equine Medicine*. Edited by Robinson, N.E., W.B. Saunders Co., 1983, pp. 405-407.
20. Van Niekerk, C.H., Loubrough, R.I., and Doms, H.W.H.: Progesterone treatment of mares with abnormal oestrus cycles early in the breeding season. *J.S. Afr. Vet. Med. Assoc.*, 44:37, 1973.
21. Squires, E.L., Stevens, W.B., McGlothlin, D.E. and Pickett, B.W.: Effect of an oral progestin on the estrous cycle and fertility of mares. *J. Anim. Sci.*, 49:729, 1979.
22. Allen, W.R., Urwin, V., Simpson, D.J., Greenwood, R.E.S., Crowhurst, R.C., Ellis, D.R., Rickets, S.W., Hunt, M.D.N., and Digby, H.R.: Preliminary studies on the use of an oral progestogen to induce oestrus and ovulation in seasonally anovulatory Thoroughbred mares. *Equine Vet. J.*, 12:141, 1980.
23. Webel, S.K., and Squires, E.L.: Control of the estrous cycle in mares with altrenogest. *J. Reprod. Fertil.*, Suppl., 32:193, 1982.
24. Loy, R.G., and Swan, S.M.: Effects of exogenous progestogens on reproductive phenomena in mares. *J. Anim. Sci.*, 25:821, 1966.
25. VanCamp, S.D.: Prolonged diestrus. In *Current Therapy in Equine Medicine*. Edited by Robinson, N.E., W.B. Saunders Co., 1983, pp. 401-402.
26. Loy, R.G., Buell, J.R., Stevenson, W., and Hamm, D.: Sources of variation response intervals after prostaglandin treatment in mares with functional corpora lutea. *J. Reprod. Fertil.*, Suppl, 27:229, 1979.
27. Hughes, J.P. and Loy, R.G.: Variations in ovulatory response associated with the use of prostaglandins to manipulate the lifespan of the normal diestrous corpus luteum of the mare. *Proc. 24th Ann. Mtg. Am. Assoc. Eq. Pract.*, 173, 1978.
28. Kiefer, B.L., Roser, J.F., Evans, J.W., Neely, D.P. and Pacheco, C.A.: Progesterone patterns observed with multiple injections of a PGF-2a analogue in the cyclic mare. *J. Reprod. Fertil.*, Suppl, 27:237, 1979.

