CONTROLLING THE ESTROUS CYCLE WITH PROGESTERONE

Matthew C. Lucy, Ph.D.
Department of Animal Sciences
University of Missouri, Columbia 65211

Introduction

Estrous synchronization in beef and dairy cattle reduces labor requirements for estrous detection and shortens the interval from calving to rebreeding. A variety of methods can be used to synchronize estrus in cattle (Patterson et al., 1989; Odde, 1990; Larson and Ball, 1992). Most methods use an injection of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$). Prostaglandin $F_{2\alpha}$ will cause regression of the corpus luteum (CL). Regression of the CL (luteolysis) is followed by the development of a preovulatory follicle, behavioral estrus, and ovulation (Lauderdale et al., 1974; Roche, 1974). Corpora lutea formed within the first five days after estrus (early-cycle CL) will not regress in response to $PGF_{2\alpha}$. A single injection of $PGF_{2\alpha}$, therefore, will only synchronize about 70% of cattle with a CL (Lauderdale, 1972).

Using Progesterone to Improve Synchrony of Estrus after $PGF_{2\alpha}$

There are several methods to improve synchrony of estrus after a single injection of $PGF_{2\alpha}$. Most of these methods involve a progestogen that is fed or implanted into cattle. Progestogens mimic the action of the CL and block ovulation. Cattle can be treated with a progestogen for 7 days before $PGF_{2\alpha}$ is administered (Macmillan and Peterson, 1993). Administration of the progestogen for 7 days before $PGF_{2\alpha}$ ensures that CL will regress in response to $PGF_{2\alpha}$ because cattle will have a CL that has developed for at least 7 days. The progestogen will also delay estrus and ovulation in cattle that naturally undergo CL regression during the progestogen treatment period before $PGF_{2\alpha}$ injection (Roche et al., 1999). The latter group of cattle will be synchronized with the rest of the breeding group.

Short-term progesterone exposure is generally achieved with an intravaginal insert (EAZI-BREED CIDR device; Pharmacia Inc. St. Louis, Missouri) or a norgestomet ear implant (Syncro-Mate-B, Sanofi Animal Health, Overland Park, KS). The CIDR device has recently been approved in the United States for beef cows, beef heifers, and dairy heifers. The insert contains progesterone that is released into the vagina and taken up by the bloodstream. Progesterone concentrations in blood after CIDR treatment are similar to those found during the estrous cycle. The Syncro-Mate-B implant is no longer available in the United States.

A second method to ensure that the CL will respond to $PGF_{2\alpha}$ is to feed cattle melengestrol acetate (MGA) before $PGF_{2\alpha}$ injection. Melengestrol acetate is typically mixed in grain and fed at 0.5 mg/head/day for 14 days. It is approved for use in beef cows and heifers. Shorter-term MGA feeding (7 days) can be used but must be combined with gonadotropin-releasing hormone (GnRH) and $PGF_{2\alpha}$ (7-11 Synch; Kojima et al., 2000). Feeding MGA for 14 days will suppress ovulation and estrus while the MGA is fed. The fertility of the estrus immediately following

MGA feeding is decreased. Therefore, cattle are not injected with $PGF_{2\alpha}$ until 17 to 19 days after the end of MGA feeding. The 17 to 19 day delay allows time for cattle to come into estrus after MGA withdrawal and develop a CL that will regress in response to $PGF_{2\alpha}$. Regression of the CL is followed by the development of a fertile preovulatory follicle, behavioral estrus, and ovulation.

Other Advantages of Progestogens

A major limitation to the success of an estrous synchronization program is the presence of anestrous cattle or prepubertal heifers in the breeding herd (Short et al., 1990; Patterson et al., 1992; Schillo et al., 1992). Progestogens offer an advantage in this regard because, in addition to improving estrous synchronization, progestogens will initiate estrus and ovulation in a percentage of prepubertal heifers and anestrous cows (Anderson et al., 1996; Fike et al., 1997; Imwalle et al., 1998). The mechanism of progestogen action on the ovary involves increased LH secretion that causes an increase in follicular development leading to ovulation (Anderson et al., 1996; Imwalle et al., 1998). The exact percentage of anestrous cattle that will ovulate in response to progestogens depends on the depth of anestrus. Cows and heifers that are in deep anestrus (i.e., unlikely to begin cycling within the next month) are unlikely to respond to progestogen treatment. Cows and heifers that are approaching estrus (i.e., will likely begin cycling within one to three weeks) will respond to progestogen treatment. As a general rule, approximately 50% of anestrus cows and prepubertal heifers will begin cycling in response to progestogen treatment.

A percentage of anestrus cows and prepubertal heifers will begin cycling in response to progestogens. Cattle diagnosed as acyclic before the treatment period, however, will have inferior reproductive performance compared to their cyclic herd mates (Lucy et al., 2001). The use of the progestogens in estrous synchronization programs can improve responses but cannot completely overcome the limitations encountered when a large percentage of the herd is anestrus or prepubertal. Herds with a large percentage of anestrous cows or prepubertal heifers at the start of the breeding season may not be able to achieve high reproductive rates during the same breeding season. Herd nutrition should be reviewed and improved during the upcoming year so that a higher proportion of cattle are cyclic during next year's breeding season.

Disadvantages of Progestogens

There is the potential for the development of persistent follicles when progestogens are used in estrous synchronization programs (Anderson and Day, 1994; Fike et al., 1999). Persistent follicles are problematic in breeding programs because oocytes from persistent follicles are inherently less healthy and cause decreased conception rate following insemination (Ahmad et al., 1995; Revah and Butler, 1996; Roche et al., 1999). Therefore, long-term progestogen treatment (> 7 days) followed by insemination at estrus (usually within 2 days after treatment) is not recommended. Short-term progestogen treatment (CIDR) in combination with $PGF_{2\alpha}$ did not affect conception rates in beef cows, beef heifers, or dairy heifers during the 3-d synchronization period or during the 31-d breeding period (Lucy et al., 2001).

Standard Protocols for Estrous Synchronization with Progestogens and $PGF_{2\alpha}$

There are simple methods to use progestogens for estrous synchronization. The first method uses a CIDR device to deliver the progestogen. The CIDR device in inserted for seven days and a luteolytic dose of $PGF_{2\alpha}$ is administered six days after CIDR insertion (Figure 1). Cattle will be in estrus one to three days after the CIDR is removed. A seven-day administration of the CIDR with an injection of $PGF_{2\alpha}$ on d 6 of insertion was an effective method for estrous synchronization in cattle (Lucy et al., 2001). Beef cows and beef and dairy heifers had improved rates of synchronized estrus compared to either $PGF_{2\alpha}$ alone or Control (no treatment). The greatest effect of the CIDR was seen immediately following CIDR withdrawal when the proportion of cattle in estrus and inseminated dramatically increased. By the end of the breeding period (31 days later), the Control or $PGF_{2\alpha}$-alone cattle generally had similar proportions of cattle in estrus and inseminated compared with CIDR+ $PGF_{2\alpha}$ groups. The difference was that most of the CIDR-treated cattle were inseminated during the first three days of the breeding period.

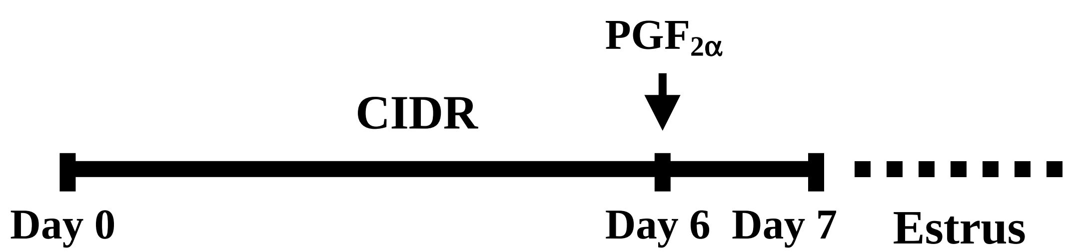

Figure 1. Simple protocol for synchronizing estrus with a CIDR device. The CIDR device is inserted for seven days and a luteolytic dose of $PGF_{2\alpha}$ is administered six days after CIDR insertion. Cattle will be in estrus one to three days after the CIDR is removed.

The protocol depicted in Figure 1 can be modified to meet the needs of individual producers. Time and labor can be saved by giving the $PGF_{2\alpha}$ injection at the same time the CIDR is removed. The synchrony of estrus will be less (about equal numbers of cows and heifers will be in estrus on days 2 and 3 after CIDR withdrawal) but fertility will not be compromised. Extending the CIDR treatment period to 8 or 9 days and giving the $PGF_{2\alpha}$ injection two days before CIDR withdrawal will increase the synchrony of estrus. The longer treatment period, however, may decrease fertility.

The CIDR device is a routine treatment for anestrus is New Zealand and Australian dairy cows. Unfortunately, the CIDR is not approved in the United States for use in lactating dairy cows. The lack of an approved progestogen represents a severe limitation to reproductive management in dairy herds with a high percentage of anestrus cows.

A second method uses MGA as a feed additive to deliver the progestogen. The MGA is fed for fourteen days and a luteolytic dose of $PGF_{2\alpha}$ is administered 17 to 19 days after MGA feeding is stopped (Figure 2). Cattle will be in estrus two to four days after the $PGF_{2\alpha}$ is administered.

Figure 2. Simple protocol for synchronizing estrus with MGA. The MGA is fed for fourteen days and a luteolytic dose of $PGF_{2\alpha}$ is administered 17 to 19 days after MGA feeding is stopped. In this example, the $PGF_{2\alpha}$ is administered 19 days after MGA feeding (day 33). Cattle will be in estrus two to four days after the $PGF_{2\alpha}$ is administered.

The original MGA- $PGF_{2\alpha}$ protocols were designed so that $PGF_{2\alpha}$ injection was given 17 days after MGA feeding was stopped. More recent data suggests, however, that giving the $PGF_{2\alpha}$ injection 19 days after MGA feeding will improve slightly estrus response and synchronized pregnancy rate (Lamb et al., 2000). The 19 day interval, therefore, is the current recommendation.

Standard Protocols for Estrous Synchronization with Progestogens, GnRH and $PGF_{2\alpha}$

Follicular growth in cattle occurs throughout the estrous cycle. Follicles grow in waves and two to three waves of follicular growth occur during each estrous cycle. Waves of follicular growth undergo distinct phases (recruitment, selection, and dominance). Dominant follicles are capable of ovulation after luteolysis. Waves can be synchronized with GnRH. The GnRH causes the dominant follicle to ovulate or turnover (become atretic). Ovulation or atresia of a dominant follicle leads to a new follicular wave (development of a new dominant follicle). The process of follicular development takes about one week. Synchronization of follicular development (waves) before $PGF_{2\alpha}$ injection improves the precision of estrous synchronization. Follicular wave synchronization also enables the use of timed insemination (see below). The CIDR protocol (Figure 1) and the MGA protocol (Figure 2) can be adapted for follicular wave synchronization (CIDR, Figure 3; MGA, Figure 4). In each case, the GnRH is given 7 days before the $PGF_{2\alpha}$ injection. Administration of the GnRH synchronizes follicular development so that estrus synchrony is improved.

Figure 3. A protocol for synchronizing estrus with a CIDR, GnRH and $PGF_{2\alpha}$. The CIDR device is inserted for seven days. The GnRH is given when the CIDR is inserted. A luteolytic dose of $PGF_{2\alpha}$ is administered when the CIDR is removed. Cattle will be in estrus one to three days after the CIDR is removed.

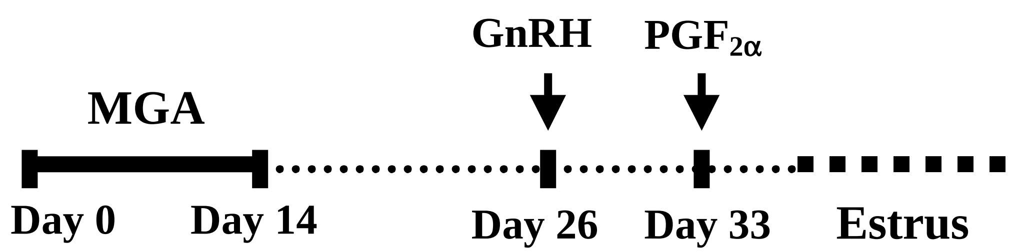

Figure 4. A protocol for synchronizing estrus with MGA, GnRH and $PGF_{2\alpha}$. The MGA is fed for fourteen days and a luteolytic dose of $PGF_{2\alpha}$ is administered 19 days after MGA feeding is stopped (day 33). GnRH is injected 7 days before the $PGF_{2\alpha}$ injection (day 26). The combination of MGA, GnRH, and $PGF_{2\alpha}$ as depicted above is called the MGA Select Protocol (Wood et al., 2001).

How to Implement Timed AI with a Combination of Progestogens, GnRH and $PGF_{2\alpha}$

Combining the above protocols (Figures 1 to 4) with some type of estrous detection aid (tail chalk, patches, electronic devices, etc.) will improve the overall response but estrous detection requires additional management and attention to details. Most producers would like to breed all cattle at a predetermined time (Timed AI). Timed AI programs are popular because herds with poor estrous detection rates can achieve superior intervals to first insemination and pregnancy when compared to cows inseminated at an observed spontaneous estrus. Cattle inseminated within timed AI programs, however, have a lower conception rate when compared to cattle inseminated at an observed spontaneous estrus. Traditional reproductive indices such as services per conception and conception rate are negatively affected when timed AI is implemented while interval to first service and overall pregnancy rate are generally improved.

Adapting the protocols depicted in Figures 3 and 4 to timed AI is simple. A second GnRH injection is given 48 to 72 hours after the $PGF_{2\alpha}$ injection (Figures 5 and 6). Cows are time inseminated either at the same time as the GnRH (Co-synch method) or 12 to 16 hours after the GnRH (Ovsynch). The overall success of the timed AI depends on a variety of factors. The most important factor may be the percentage of cycling cows at the start of treatment (Lamb et al., 2001).

Figure 5. A protocol for timed AI (TAI) with a CIDR, GnRH and $PGF_{2\alpha}$. The CIDR device is inserted for seven days. A GnRH injection is given when the CIDR is inserted. A luteolytic dose of $PGF_{2\alpha}$ is administered when the CIDR is removed. Cattle are given GnRH and inseminated 48 hours after the $PGF_{2\alpha}$ injection (Lamb et al., 2001).

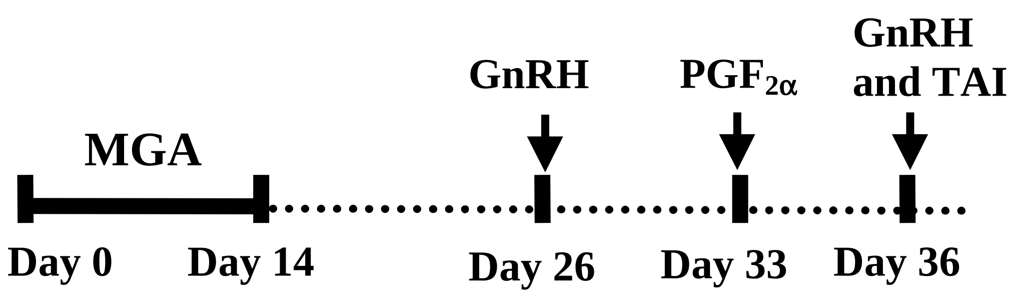

Figure 6. A protocol for timed AI (TAI) with MGA, GnRH and $PGF_{2\alpha}$. The MGA is fed for fourteen days and a luteolytic dose of $PGF_{2\alpha}$ is administered 19 days after MGA feeding is stopped (day 33). GnRH is injected 7 days before the $PGF_{2\alpha}$ injection (day 26). Cattle are given GnRH and inseminated 72 hours after the $PGF_{2\alpha}$ injection (Perry et al., 2001).

Synchronization of Second Service

Estrous synchronization is a good way to control the time of first insemination. Only about 50% of beef cows and 30% of dairy cows, however, will be pregnant after first insemination. The fate of the 50 to 70% of cattle that are open after first insemination usually depends on detecting the return to estrus after the pregnancy fails. The timing of second estrus after insemination is variable because many cows have an embryo that dies around the time of maternal recognition of pregnancy and the normal luteolytic mechanisms are delayed. The fact that inseminated cows represent a mixture of pregnant and nonpregnant cows and that nonpregnant cows have a variable return to estrus complicates methods that can be used to synchronize second service. Very few reliable methods are available for resynchronizing second service in United States. One successful method was to insert a CIDR device from 17 to 22 days after first insemination (Van Cleeff et al., 1996). The CIDR device synchronizes the return to estrus because cattle returning 17 and 22 days after insemination are held out of estrus until after the CIDR is removed. Their estruses are synchronized after CIDR removal.

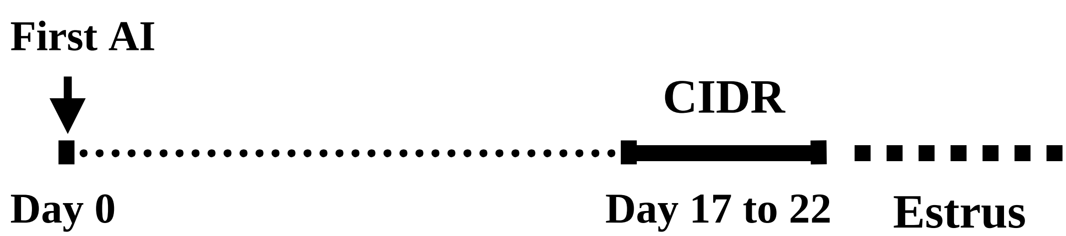

Figure 7. A protocol for synchronizing second estrus with a CIDR. The CIDR device is inserted from day 17 to 22 after first insemination (AI). Nonpregnant cattle will be in estrus two to three days after the CIDR is removed and can be inseminated.

Conclusions

Estrous synchronization reduces labor requirements for estrous detection, shortens the interval from calving to rebreeding and increases the rate of implementation of artificial insemination in beef and dairy herds. Methods for estrous synchronization should be relatively simple and should be robust so that they can be applied under a variety of management conditions. Progestogens are important components of estrous synchronization systems because they improve overall responses. Improvements in estrous synchronization with progestogens occur because anestrous cattle are induced into cyclicity, early-cycle CL are given time to become $PGF_{2\alpha}$-responsive, and late-cycle cattle are held out of estrus until progestogen withdrawal. Adding follicular synchronization and GnRH-induced ovulation to progestogen-based programs enables the use of timed AI. Progestogens can also be used to synchronize estrus in second service cattle. Additional use of progestogens-based estrous synchronization programs in the cattle industry should improve efficiency and profitability of cattle herds.

References

Ahmad, N., F. N. Schrick, R. L. Butcher, and E. K. Inskeep. 1995. Effect of persistent follicles on early embryonic losses in beef cattle. Biol. Reprod. 52:1129-1135.

Anderson, L. H., and M. L. Day. 1994. Acute progesterone administration regresses persistent dominant follicles and improves fertility of cattle in which estrus was synchronized with melengestrol acetate. J. Anim. Sci. 72:2955-2961.

Anderson, L. H., C. M. McDowell, and M. L. Day. 1996. Progestin-induced puberty and secretion of luteinizing hormone in heifers. Biol. Reprod. 54:1025-1031.

Fike, K. E., M. L. Day, E. K. Inskeep, J. E. Kinder, P. E. Lewis, R. E. Short, and H. D. Hafs. 1997. Estrus and luteal function in suckled beef cows that were anestrus when treated with an intravaginal device containing progesterone with or without a subsequent injection of estradiol benzoate. J. Anim. Sci. 75:2009-2015.

Fike, K. E., M. E. Wehrman, B. R. Lindsey, E. G. Bergfeld, E. J. Melvin, J. A. Quintal, E. L. Zanella, F. N. Kojima, and J. E. Kinder. 1999. Estrus synchronization of beef cattle with a combination of melengestrol acetate and an injection of progesterone and 17β-estradiol. J. Anim. Sci. 77:715-723.

Imwalle, D. B., D. J. Patterson, and K. K. Schillo. 1998. Effects of melengestrol acetate on onset of puberty, follicular growth, and patterns of luteinizing hormone secretion in beef heifers. Biol. Reprod. 58:1432-1436.

Kojima, F.N., B.E. Salfen, J.F. Bader, W.A. Ricke, M.C. Lucy, M.F. Smith, and D.J. Patterson. 2000. Development of an estrus synchronization protocol for beef cattle with short-term feeding of melengestrol acetate: 7-11 synch. J. Anim. Sci. 78:2186-2191.

Lamb, G.C., J.S. Stevenson, D.J. Kesler, H.A. Garverick, D. R. Brown, and B.E. Salfen. 2001. Inclusion of an intravaginal progesterone insert plus GnRH and prostaglandin $F_{2\alpha}$ for ovulation control in postpartum suckled beef cows. J. Anim. Sci. 79:2253-2259.

Lamb, G.C., D.W. Nix, J.S. Stevenson, and L.R. Corah. 2000. Prolonging the MGA-prostaglandin $F_{2\alpha}$ interval from 17 to 19 days in an estrus synchronization system for heifers. Theriogenology 53:691-698.

Larson, L. L., and P. J. H. Ball. 1992. Regulation of estrous cycles in dairy cattle: a review. Theriogenology 38:255-267.

Lauderdale, J. W. 1972. Effects of $PGF_{2\alpha}$ injection on pregnancy and estrous cycle of cattle. J. Anim. Sci. 35:246 (Abstr.).

Lauderdale, J. W., B. E. Seguin, J. N. Stellflug, J. R. Chenault, W. W. Thatcher, C. K. Vincent, and A. F. Loyancano. 1974. Fertility of cattle following $PGF_{2\alpha}$ injection. J. Anim. Sci. 38:964-967.

Lucy, M.C., H.J. Billings, W.R. Butler, L.R. Ehnis, M.J. Fields, D.J. Kesler, J.E. Kinder, R.C. Mattos, R.E. Short, W.W. Thatcher, R.P. Wettemann, J.V. Yelich, and H.D. Hafs. 2001. Efficacy of an intravaginal progesterone insert and an injection of $PGF_{2\alpha}$ for synchronizing estrus and shortening the interval to pregnancy in postpartum beef cows, peripubertal beef heifers, and dairy heifers. J. Anim Sci. 79:982-995.

Macmillan, K. L., and A. J. Peterson. 1993. A new intravaginal progesterone releasing device for cattle (CIDR-B) for oestrous synchronization, increasing pregnancy rates, and the treatment of post-partum anestrus. Anim. Reprod. Sci. 33:1-25.

Odde, K. G. 1990. A review of synchronization of estrus in postpartum cattle. J. Anim. Sci. 68:817-830.

Patterson, D. J., G. H. Kiracofe, J. S. Stevenson, and L. R. Corah. 1989. Control of the bovine estrous cycle with melengestrol acetate (MGA): a review. J. Anim. Sci. 67:1895-1906.

Patterson, D. J., R. C. Perry, G. H. Kiracofe, R. A. Bellows, R. B. Staigmiller, and L. R. Corah. 1992. Management considerations in heifer development and puberty. J. Anim. Sci. 70:4018-4035.

Perry, G.A., J.F. Bader, M.F. Smith, and D.J. Patterson. 2001. Evaluation of a fixed-time artificial insemination protocol for beef cows. J. Anim. Sci. 79(Suppl. 1):462.

Revah, I., and W. R. Butler. 1996. Prolonged dominance of follicles and reduced viability of bovine oocytes. J. Reprod. Fertil. 106:39-47.

Roche, J. F. 1974. Synchronization of oestrus and fertility following artificial insemination in heifers given prostaglandin $F_{2\alpha.}$ J. Reprod. Fertil. 37:135-138.

Roche, J. F., E. J. Austin, M. Ryan, M. O'Rourke, M. Mihm, and M. G. Diskin. 1999. Regulation of follicle waves to maximize fertility in cattle. J. Reprod. Fertil. Suppl. 54:61-71.

Schillo, K. K., J. B. Hall, and S. M. Hileman. 1992. Effects of nutrition and season on the onset of puberty in the beef heifer. J. Anim. Sci. 70:3994-4005.

Short, R. E., R. A. Bellows, R. B. Staigmiller, J. G. Berardinelli, and E. E. Custer. 1990. Physiological mechanisms controlling anestrus and infertility in postpartum beef cattle. J. Anim. Sci. 68:799-816.

Van Cleeff J., K.L. Macmillan, M. Drost, M.C. Lucy, and W.W. Thatcher. 1996. Effects of administrating progesterone at selected intervals after insemination of synchronized heifers on pregnancy rates and resynchronization of returns to service. Theriogenology 46:1117-1130.

Wood, S.L., M.C. Lucy, M.F. Smith, and D.J. Patterson. 2001. Improved synchrony of estrus and ovulation with addition of GnRH to a melengestrol acetate-prostaglandin $F_{2\alpha}$ synchronization treatment in beef heifers. J. Anim Sci. 79:2210-2216.