Synchronization of Estrus

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Estrous synchronization gives many beef cattle producers the opportunity to capture the economic benefits of artificial insemination (AI). Because AI involves a substantial investment of labor and time, most commercial farms or ranches will not utilize this technology unless this investment can be confined to a period of less than 5 to 7 days. To make the labor requirements of AI compatible with modern beef cattle breeding, the estrous cycle must be synchronized so that a high percentage of treated females show a fertile, closely synchronized estrus. The synchronization of cattle can be achieved by the use of progestogens,[1] progestogen-prostaglandin combinations,[2] prostaglandins alone,[3] progestogen-estrogen combinations,[4,5] and gonadotropin-prostaglandin combinations with or without progestogens.[6]

In order to understand how each of these hormones, and the programs that have been developed around them, work in individual animals and on a herd basis, one must review the physiology of the bovine estrous cycle.

Synchronization of estrus utilizing progestogens

For many years, progestogens have been known to suppress estrus in cattle and were the first products used in an attempt to control the estrous cycle. Zimbelman et al. (1970)[7] reviewed 24 studies that addressed the effectiveness of the progestogen, melengestrol acetate (MGA) as an estrus synchronization agent. They showed a 14% reduced first service conception percentage in treated females compared to controls when MGA was fed for 10 to 18 days. Fertility has also been shown to be reduced after long-term administration of other progestogens such as: 6-methyl-17 acetoxy-progesterone (MAP),[8] 6-chloro-♠^{6}-dehydro-17-acetoxyprogesterone (CAP),[9] and dihydroxyprogesterone acetophenide (DHPA).[10] Treatment of cattle with progestogens for less than 14 d was reported not to reduce conception percentage.[11,12,13] In addition, short-term exposure to progestogens causes some anestrus (postpartum or prepubertal) cattle to begin cycling. However, for these short-term progestogen systems to be effective in synchronizing estrus, a luteolytic agent must be incorporated.

Synchronizing estrus utilizing progestogen plus prostaglandin $F_{2\propto}$

Prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) and its analogs cause luteolysis and a return to estrus in cattle when given during the luteal phase (Days 5 to 17; Day 0=estrus) of the estrous cycle[14,15] and the fertility of the induced estrus is normal.[12,16,17] Research has shown that a higher percentage of cattle treated with PGF during the late luteal phase (Days 10 to 17) exhibited estrus than those treated during the early luteal phase (Days 5 to 9).[18,19] It has also been shown that the closest synchrony of estrus occurs when cattle are at a similar stage of the estrous cycle when $PGF_{2\alpha}$ is administered.[18] Based on the results of these research trials, a system that initially synchronizes heifers by feeding MGA and then administers $PGF_{2\propto}$ during the late luteal phase of the subsequent cycle should produce a high percentage of heifers displaying closely synchronized estrus and with improved fertility.

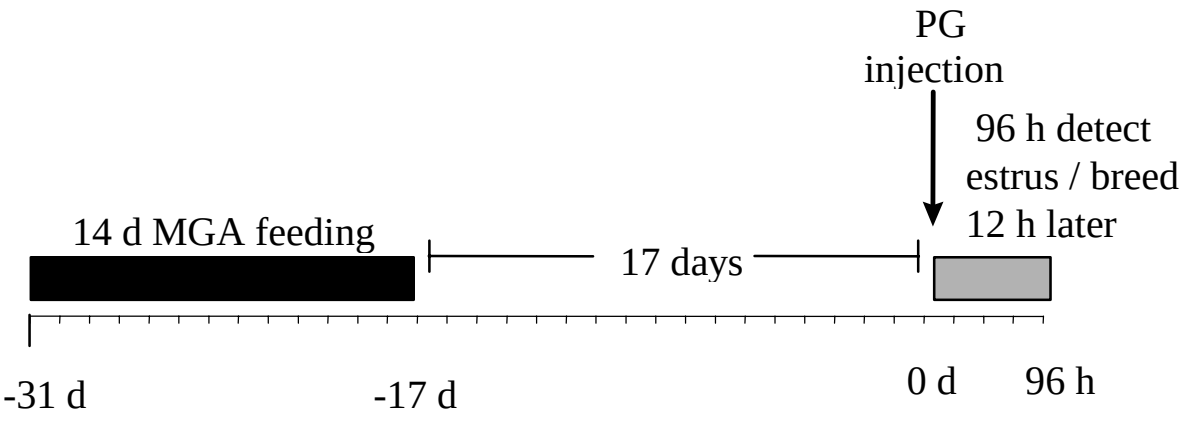

Figure 4. Melengestrol acetate (MGA) administered orally in the feed can be combined with prostaglandin $F_{2\alpha}$ (PG) and used as an estrous synchronization and puberty induction system for heifers. Heifers are observed for estrous behavior for 96 hours after PGF treatment. Any heifer displaying signs of estrus is identified and bred artificially 12 hours after first detection of estrous behavior.

Colorado researchers developed a system in which MGA is fed for 14 d, followed by administration of $PGF_{2\propto}$ 17-19d after the last day of MGA feeding. By waiting 17 d before inducing luteolysis with $PGF_{2\propto}$, the researchers overcame the problem of reduced fertility after feeding MGA. This system also takes advantage of the fact that $PGF_{2\propto}$ is more effective when administered late (Days 10 to 17) in the estrous cycle than when given early (Days 5 to 9) in the estrous cycle (Figure 4).[20] However, to be effective, the MGA must be consumed on a daily basis. If consumption is erratic, estrus will not be synchronized throughout the group of females.

One impediment to the widespread use of estrus synchronization and AI among producers is the amount of time and expertise required to accurately detect heifers in estrus. Timed-insemination, where artificial insemination is scheduled for an appointed time after synchronization is designed to decrease this time commitment and expertise. Breeding at an appointed time without regard to estrous behavior following the Colorado system of MGA/$PGF_{2\propto}$ estrous synchronization, has been shown to give satisfactory

pregnancy percentages in cycling heifers (serum progesterone > 1 ng/mL at time of $PGF_{2\alpha}$ administration).[21] Cycling heifers time-inseminated at 72 h after $PGF_{2\alpha}$ administration had a conception percentage of 50.8% compared to a conception percentage of 66.7% for cycling heifers detected in estrus and bred 12 hours later.[21] However, because all heifers in the timed-insemination group were inseminated artificially versus only those heifers detected in estrus in the estrus-detected group, 50.8% of the heifers in the timed-inseminated group became pregnant to AI, compared to 42.7% of the estrus-detected group. This indicates that the timed-insemination was successful in causing conception in heifers that ovulated at a time consistent with the synchronization system but had not been detected in estrus. This was confirmed by the fact that 39.1% of the heifers that were considered cyclic, based on serum P_4 above 1 ng/ml at the time of $PGF_{2\alpha}$ administration, but that were not detected in estrus, did become pregnant to the timed AI.[21] Others found that the percentage of puberal heifers, as determined by P_4 analysis, that failed to exhibit estrus within 6 d of MGA/$PGF_{2\alpha}$ treatment and within 21 d for the nonsynchronized controls were 17.1 and 15.3%, respectively.[22]

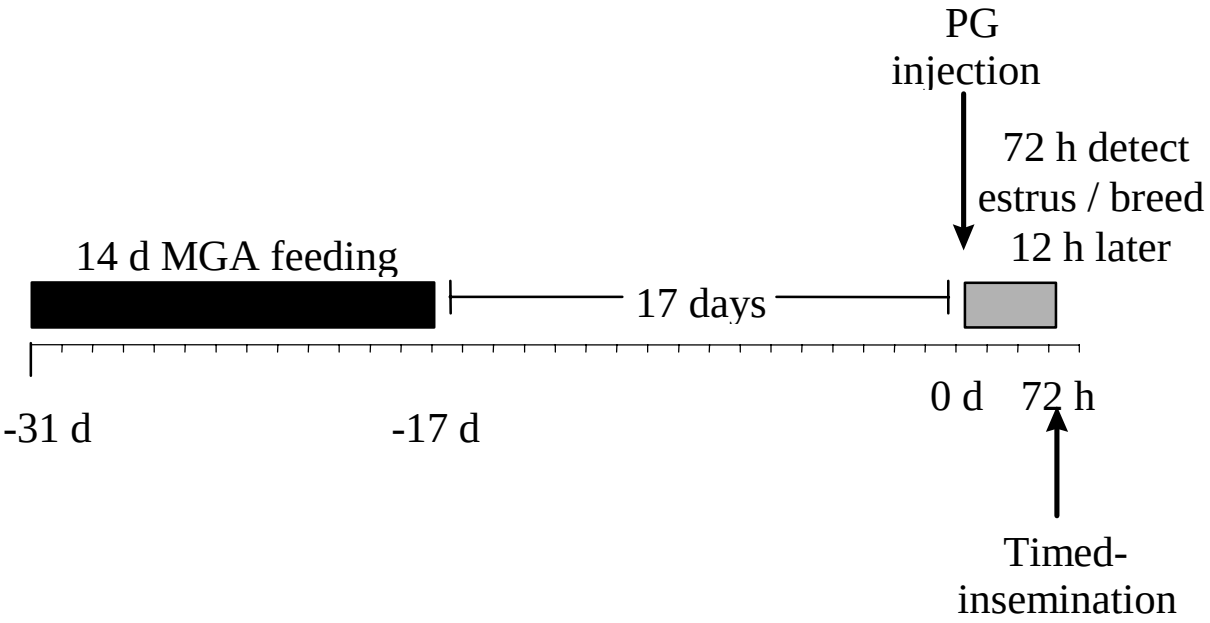

Figure 5. Melengestrol acetate (MGA) administered orally in feed can be combined with prostaglandin $F_{2\alpha}$ (PG) and used as an estrous synchronization and puberty induction system for heifers where estrous detection followed by insemination 12 hours later is combined with timed-insemination 72 hours after PG administration. Heifers are observed for estrous behavior for 72 hours after PG treatment. Any heifer displaying signs of estrus is identified and bred artificially 12 hours after first detection of estrous behavior. At 72 hours after PG treatment, all heifers not bred are inseminated artificially regardless of success or failure in being detected in estrus.

A system to maximize the number of heifers pregnant to AI in a 3-day period of time utilizes both estrus detection and timed-insemination.[21] After synchronizing estrus in heifers with the MGA/$PGF_{2\alpha}$ system, producers can utilize detection of estrus followed

by insemination 12 hours later for the first 72 hours after $PGF_{2\alpha}$ administration combined with timed-insemination at 72 h after $PGF_{2\alpha}$ (Figure 5). This system capitalizes on the higher conception percentage found in heifers that are bred 12 h after detected in estrus, as well as capitalizing on the advantage of timed-insemination for settling heifers that ovulate in conjunction with the synchronization system but who are not detected in estrus.

Synchronizing estrus utilizing progestogen plus prostaglandin - CIDR®

Recently, beef producers in the U.S. gained a new tool to be used in estrus synchronization programs. This tool is called a CIDR It is a T-shaped devise that is about 5 inches long that is inserted into the vagina of breeding females. The CIDR releases progesterone, which is absorbed into the blood stream.

CIDRs were developed in New Zealand and have been used there and in other countries for several years with good results. The wings of the CIDR are pulled in so that the entire device is shaped like a rod that can be inserted into the vagina with an applicator. On the end opposite the wings, a tail is attached that hangs outside the heifer and allows you to easily remove the insert seven days after administration. The backbone of the CIDR is a nylon spine covered by a progesterone impregnated silicone skin. Upon insertion, blood progesterone concentration rise rapidly. Maximal concentrations are reached within an hour. Progesterone concentrations are maintained at a relatively constant level during the seven days the insert is in the vagina. Upon removal of the insert, progesterone concentration in the bloodstream drops quickly.

Very few CIDRs fall out during the 7-day treatment. The average loss is only 2-3% in most herds with a few reaching 10%. Research with dairy cows has shown that while most cows with a CIDR insert will have a clear to cloudy mucus discharge from the vagina due to mild irritation of the vaginal wall, very few (2%) had evidence of a vaginal infection.

The schedule that should be followed is:

Day 1 – Insert the CIDR device into the vagina of heifers or cows to be bred. This device will be left in place for 7 days.

Day 7 – All cows and heifers to be bred are injected with a 5 cc dose of Lutalyse intramuscularly in the neck.

Day 8 – The CIDR is removed. The animal's head does not necessarily need to be caught to remove the device. Often confinement in a crowding alley will be sufficient.

Days 9-11 – Observe for signs of heat and inseminate following detection of heat.

Some veterinarians have altered this schedule by giving the Lutalyse injection on the same day that the CIDR is removed. The Lutalyse injection should be administered into the neck muscles with a 1½ inch, 16 gauge needle.

CIDRs are labeled for use in the synchronization of both beef cows and heifers (as well as dairy heifers). They are also labeled for their ability to cause suckled beef

cows to show estrus sooner after calving, and will cause replacement heifers to express heat at a younger age and weight.

Research using CIDRs in beef heifers and cows was conducted over several years at a number of universities around the country. A report that summarized those trials indicates that use of CIDRs did not decrease fertility compared to untreated females and was successful in inducing almost 50% of non-cycling females to show signs of a fertile heat following removal of the CIDR in the herds tested.

To avoid problems with CIDR use, individuals handling the device should wear rubber or latex gloves to prevent exposure to the progesterone and to reduce the chance of carrying contamination from your hands into the vagina of the cow or heifer. Cleanliness is very important to avoid vaginal infections. The inserts available in the U.S. have a lower dose of progesterone than inserts in other countries. For this reason, and to enhance cleanliness and decrease the chance for disease transfer between animals, reusing CIDRs is not advisable.

If a CIDR device is left in an animal longer than 7 days, fertility to subsequent breeding will start to decline. If a CIDR device is accidentally placed in a pregnant cow or heifer, no problems will occur due to the CIDR itself, but injection of Lutalyse will cause abortion in many animals. There is no slaughter withdrawal for either Lutalyse or CIDRs.

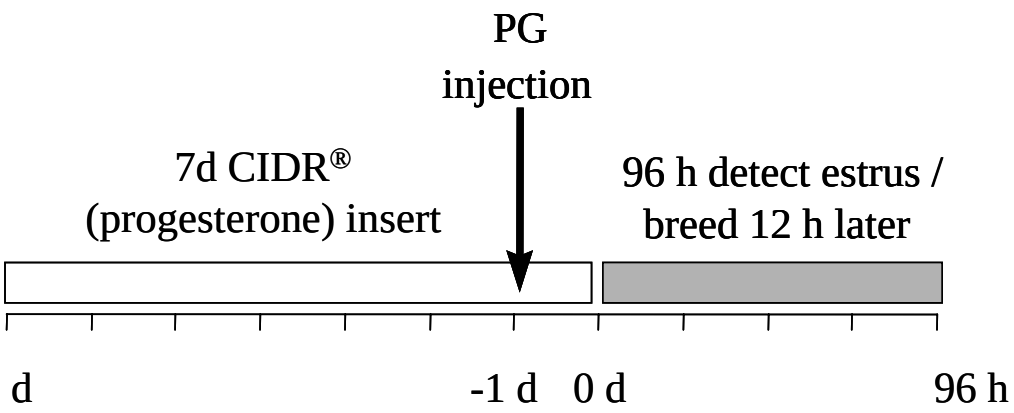

Figure 6. Progesterone can be combined with prostaglandin $F_{2\alpha}$ (PG) and used as an estrous synchronization system (CIDR®) for heifers and cows. An insert containing progesterone is placed intravaginally. The CIDR device is left in place for seven days before being removed. One day prior to the removal of the norgestomet implant, PG is administered. Heifers are observed for estrous behavior for 96 hours after PG treatment. Any heifer displaying signs of estrus is identified and bred artificially 12 hours after first detection of estrous behavior.

Synchronizing estrus utilizing prostaglandin $F_{2\alpha}$ alone

The exact mechanism of action of $PGF_{2\alpha}$ on the corpus luteum (CL) is not known; however, it probably acts to disrupt delivery of LH to the CL, or by negatively affecting LH receptors in the CL. Injecting $PGF_{2\alpha}$ causes luteolysis and a corresponding decrease in progesterone levels in the circulation. Decreasing progesterone concentrations allow the final maturation of the ovulating follicle and then expression of estrus followed by ovulation. This series of events is indistinguishable from the normal events surrounding the endogenous release of $PGF_{2\alpha}$ that occurs around day 17 of the estrous cycle. Prostaglandin $F_{2\alpha}$ as well as an analog are currently available and labeled for use in the bovine for estrous synchronization. Assuming that about the same number of heifers in a group exhibit estrus each day, 55% of cycling heifers should have a CL that would respond to an injection of $PGF_{2\alpha}$ (heifers in d 5-16 of the estrous cycle), 45% of heifers
either have "young CLs" (less than d 5 of the estrous cycle) or are already

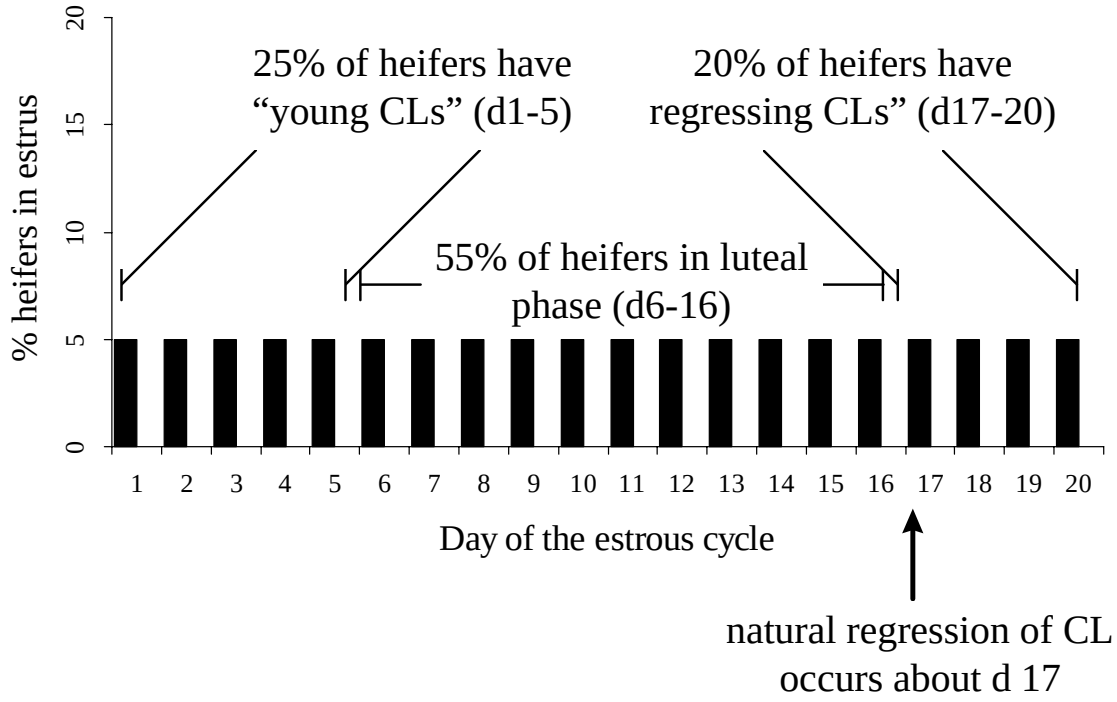

Figure 7. Assuming a 20-day estrous cycle for heifers, 5% of cycling heifers within a group should display estrus on any given day. This places about 25% of heifers within a group that will not be expected to respond to prostaglandin $F_{2\alpha}$ (PG) because they have ovulated within five days and have a "young CL" that is refractory to the lytic effect of PG. Fifty-five percent of cycling heifers should respond to PG by undergoing CL lysis because these heifers are in the mid- to late-luteal phase of the estrous cycle. The remaining 20% of cycling heifers within a group would appear to respond to PG administration by returning to estrus within 1 to 4 days, but actually, these heifers are responding to natural, spontaneous CL lysis and would have displayed estrus in 1 to 4 days regardless of PG treatment.

undergoing spontaneous CL regression (d 17-20). Both the group of heifers that undergoes luteolysis due to the $PGF_{2\alpha}$ treatment, plus the group that undergoes spontaneous CL regression should display estrus and should ovulate a fertile oocyte within 96 hours of a single $PGF_{2\alpha}$ injection (75% of cycling heifers in a group; Figure 7).

Several management strategies can be utilized to increase the percentage of $PGF_{2\alpha}$-treated heifers that respond at a predetermined time that is convenient for the producer.

One strategy is to observe the heifers for 5 or more days and to identify those who display indications of estrus. Identified heifers are bred artificially 12 hours after first being detected in estrus. At the end of the 5-day observation period, the remaining heifers are treated with $PGF_{2\alpha}$. At this time, one should feel confident that the remaining cycling heifers are past day 5 of the estrous cycle, and when injected with $PGF_{2\alpha}$, they should either have a CL that will respond to $PGF_{2\alpha}$, or will be at a stage in the estrous cycle that is undergoing spontaneous CL regression. Observation for estrous behavior is continued for at least 96 hours with insemination occurring 12 hours after first detection of estrus (Figure 8). The advantage of this system is that use of $PGF_{2\alpha}$ is minimized in that only heifers that are likely to respond are injected. The disadvantage is that the length of time committed to estrous detection and AI is at least 9 days.

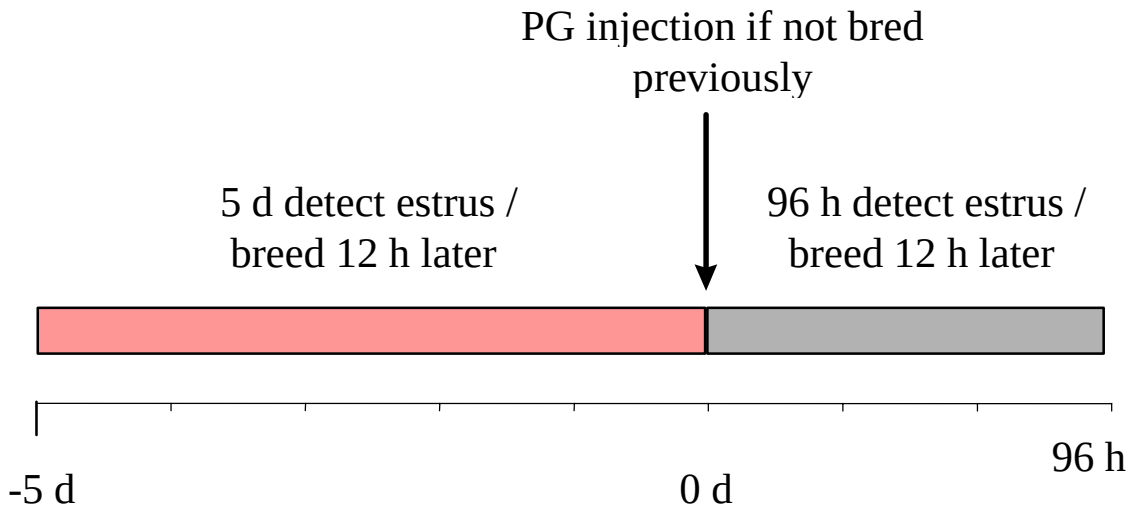

Figure 8. Prostaglandin $F_{2\alpha}$ (PG) used alone can act to synchronize estrus in groups of heifers. One method is to observe the heifers for indications of estrus for 5 days - any heifer displaying signs of estrus is identified and bred artificially 12 hours later. After five days, all heifers not previously bred are injected with PG. All cycling heifers injected should be ready to undergo natural CL lysis, (beyond day-5 of the estrous cycle) and should have a CL that will respond to PG by lysing. Heifers are observed for estrous behavior for 96 hours after PG treatment. Any heifer displaying signs of estrus is identified and bred 12 hours after first detection of estrous behavior.

Another strategy is to treat all heifers in a group with $PGF_{2\alpha}$, observe for estrous behavior, and breed artificially 12 hours after detection for at least 96 hours. During this first treatment, one would expect to breed 75% of the heifers (if all the heifers are cycling, all the heifers respond to the $PGF_{2\alpha}$ treatment, and all the responding heifers are detected in estrus). Then, 11 to 14 days after the first $PGF_{2\alpha}$ injection, another treatment is given. At this time, the remaining 25% of heifers should be in the 11^{th} to 16^{th} day of the estrous cycle. Observation for estrous behavior and breeding is done as before (Figure 9). One advantage of this system is that the length of time committed to the program is reduced to 8 days of estrus detection and AI. The other advantage is that the second injection allows a second chance to breed artificially those heifers that are cycling but who failed to respond to the $PGF_{2\alpha}$ treatment or were not detected in estrus.

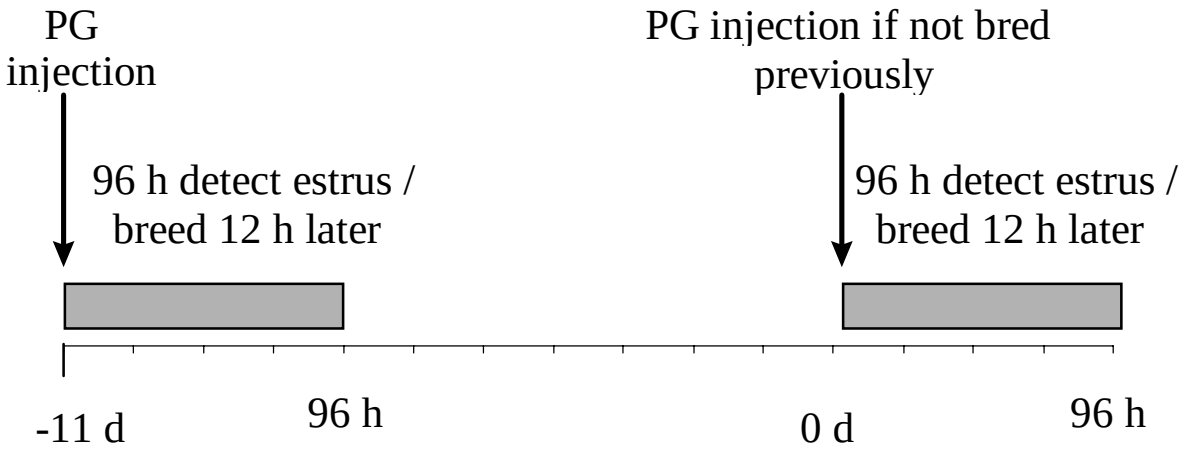

Figure 9. A second method where Prostaglandin $F_{2\alpha}$ (PG) is used alone can act to synchronize estrus in a group of heifers is to inject all heifers in group with PG and observe the heifers for indications of estrus for 96 hours - any heifer displaying signs of estrus is identified and bred artificially 12 hours after first detection of estrous behavior. Heifers that are in days 0 to 5 of the estrous cycle are not expected to respond to the PG treatment. Therefore, in order to have an opportunity to breed those heifers as well as any heifers that were not detected in estrus but who ovulated at a time consistent with the initial PG injection, a second injection of PG is given 11 to 14 days after the first. Again, heifers are observed for estrous behavior for 96 hours after PG treatment. Any heifer displaying signs of estrus is identified and bred artificially 12 hours after first detection of estrous behavior.

The final strategy that is commonly utilized involves two injections of $PGF_{2\alpha}$ administered 11 to 14 days apart (Figure 10).[10,16,23] No estrous detection or breeding is done after the first injection, and all heifers, regardless of whether or not they responded to the first treatment are given the second injection. The 75% of cycling heifers that should respond to the first injection within 96 hours are on days 6 to 14 of the estrous cycle at the time of the second injection. The 25% of cycling heifers that are not expected to respond to the first injection because they have “young CLs” (<5 days past ovulation)

are on days 10 to 19 of the estrous cycle at the second injection. Therefore, by utilizing two injections, 100% of the heifers should be at a stage of the estrous cycle that will allow them to respond to the second PGF injection. Observation of heifers for indications of estrous behavior followed by artificial insemination 12 hours after first detection follows the second $PGF_{2\alpha}$ treatment for at least 96 hours. The advantage of this system is that only 4 days are required for estrus detection and AI. The disadvantage is the increased cost, labor, and management that results from the fact that all the heifers are handled twice for $PGF_{2\alpha}$ treatments, as well as being handled once for insemination. And, although sound theoretically, the effectiveness of synchronization and pregnancy percentages are not always acceptable following this method.[25,26,27] However, synchronization and pregnancy percentages are improved when the injections are 14 days apart rather than on an 11 day interval.[28]

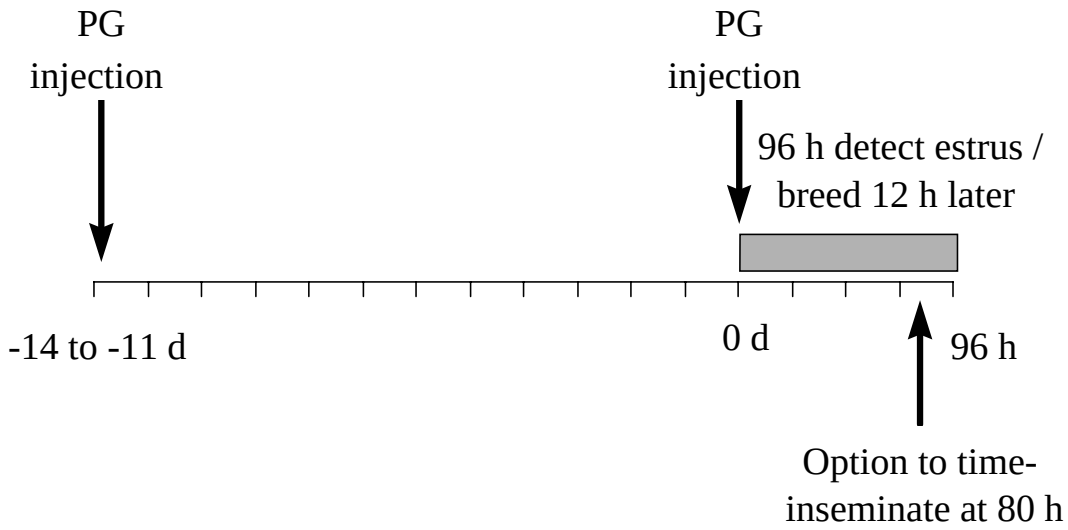

Figure 10. Prostaglandin $F_{2\alpha}$ (PG) used alone can act to synchronize estrus in groups of heifers. One method is to inject all heifers in group with PG twice at a 11- to 14-day interval. After the first injection, 75% of treated, cycling heifers should display estrous behavior either because of PG-induced lysis of the CL, or because of natural, spontaneous CL lysis at the end of the luteal phase of the estrous cycle. However, heifers are not bred after this first treatment. The second injection of PG, approximately 11-14 days after the first, should result in all cycling heifers responding to the PG treatment. Heifers are observed for estrous behavior for 96 hours after PG treatment. Any heifer displaying signs of estrus is identified and bred artificially 12 hours after first detection of estrous behavior. Timed-insemination 80 hours after PG administration has been described, although results have not been as successful following either timed-insemination or insemination following estrus detection as some other methods of estrous synchronization.

Timed-insemination, or breeding at a preset appointment 80 hours after the second injection of $PGF_{2\alpha}$ when following the two-injection method regardless of estrus response, has been described.[3] However, conception percentages are lower than if heifers

are only bred if detected in estrus. Therefore, clients should either be advised not to utilize timed-insemination following treatments with $PGF_{2\propto}$ alone, or to expect lower pregnancy percentages compared to insemination following detected estrus, or when utilizing timed-insemination when combining $PGF_{2\propto}$ and progestogens or gonadotropins.

Synchronizing estrus utilizing GnRH plus prostaglandin $F_{2\propto}$

Another method of synchronization is the combination of Gonadotropin releasing hormone (GnRH) and $PGF_{2\propto}$. The protocol involves an injection of GnRH followed 7 days later by an injection of $PGF_{2\propto}$. A second injection of GnRH follows the $PGF_{2\propto}$ injection by 30 to 48 hours. The method is designed to be used with timed insemination 8 to 24 hours after the last GnRH injection (Figure 11).[6,33,34] This synchronization system results in a tight synchrony of estrus, allowing breeding at an appointed time without detection of estrus. The first injection of GnRH causes either ovulation or luteinization of all dominant or large growing follicles. As a result, a new follicular wave is initiated in all cows about 3 days after the injection. Therefore, all the females in the group have growing follicles of about the same stage of development. In addition, GnRH stimulates development of luteal tissue from the cells that were previously the dominant follicle. The $PGF_{2\propto}$ injection lyses the CL resulting from the GnRH injection that initiates the process that leads to ovulation. And, the final GnRH injection serves to increase the synchrony of ovulation within the group of females. The success of the first injection of GnRH to synchronize follicular growth is very good in cows, but less in heifers.[33,34]

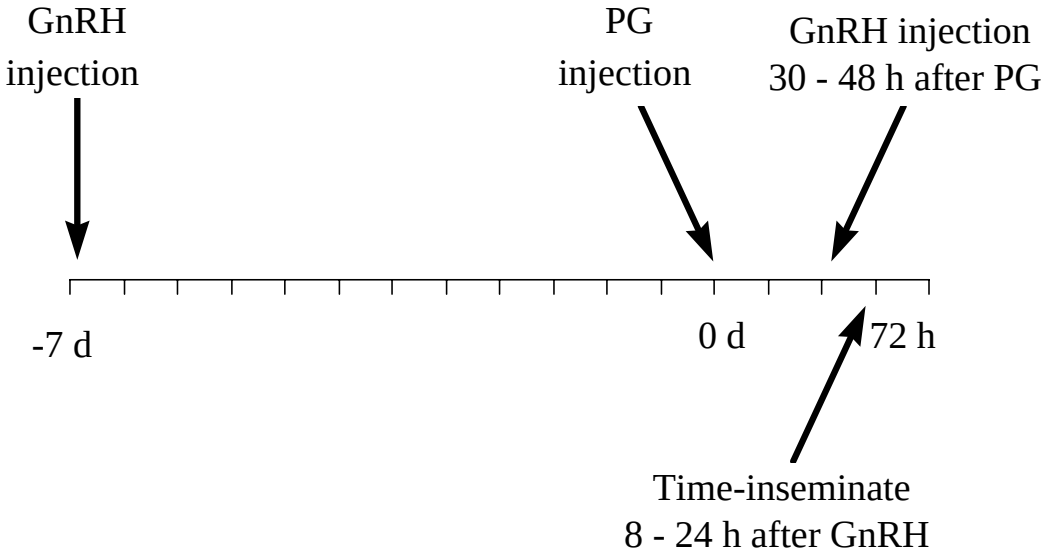

Figure 11. This method utilizes an initial dose of GnRH to synchronize ovulation in a group of females. The Prostaglandin $F_{2\alpha}$ (PG) injection given 7 days later lyses the resulting CL. The second GnRH injection given 30 to 48 hours after PGF increases the synchrony of ovulation so that timed-insemination can be utilized 8 to 24 hours later.

A modification of the GnRH-PG system designed to be used with timed insemination is a system whereby the second GnRH injection is not given and

insemination follows estrous detection. Because 5 to 15% of females treated with GnRH will exhibit estrus prior to the time of the PG injection 7 days later, estrus detection should begin about 4 days after the GnRH injection and should continue for 4 days past the PG injection. This system is easy to implement with only 3 trips through the squeeze chute and it captures the advantage of initiation cycling in some anestrous postpartum cows and prepuberal heifers as the result of GnRH administration.

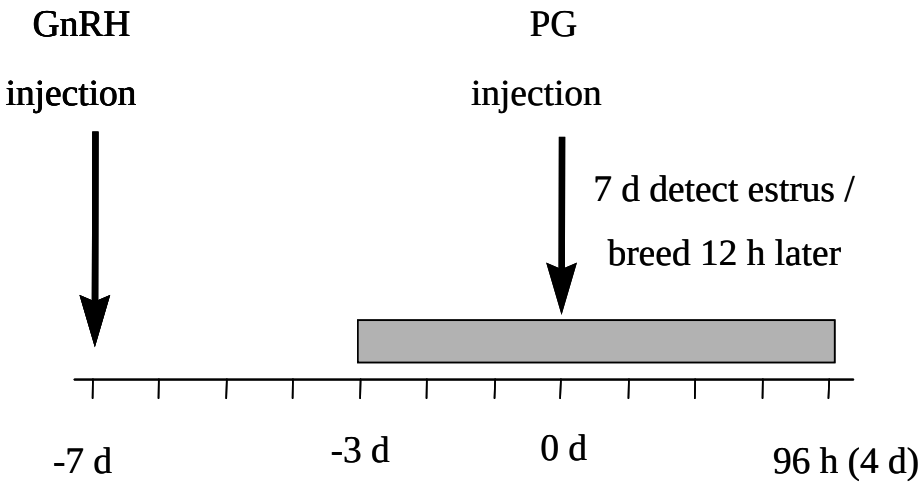

Figure 12. A modification of the method illustrated in Figure 11 utilizes an initial dose of Gonadotropin-releasing hormone (GnRH) to synchronize ovulation in a group of heifers followed by a Prostaglandin $F_{2\alpha}$ (PG) injection given 7 days later to lyse the resulting CL. The second GnRH injection given 30 to 48 hours after PG in Figure 11 is omitted, and rather than utilizing timed-insemination, the females are observed for estrous behavior for beginning 4 days after GnRH treatment and continuing for 4 days past the PG injection. Any female displaying signs of estrus is identified and bred artificially 12 hours after first detection of estrous behavior.

Synchronizing estrus utilizing progestogen and prostaglandin $F_{2\alpha}$ plus GnRH

Adding an injection of GnRH to synchronization systems that utilize feed-grade progestogen (MGA) and prostaglandin $F_{2\alpha}$ (PG) appears to slightly improve the percentage of females that exhibit estrus and causes the animals that exhibit estrus to do so in a shorter time span (Figure 13). With this modification, GnRH is injected 7 days prior to the PG injection.

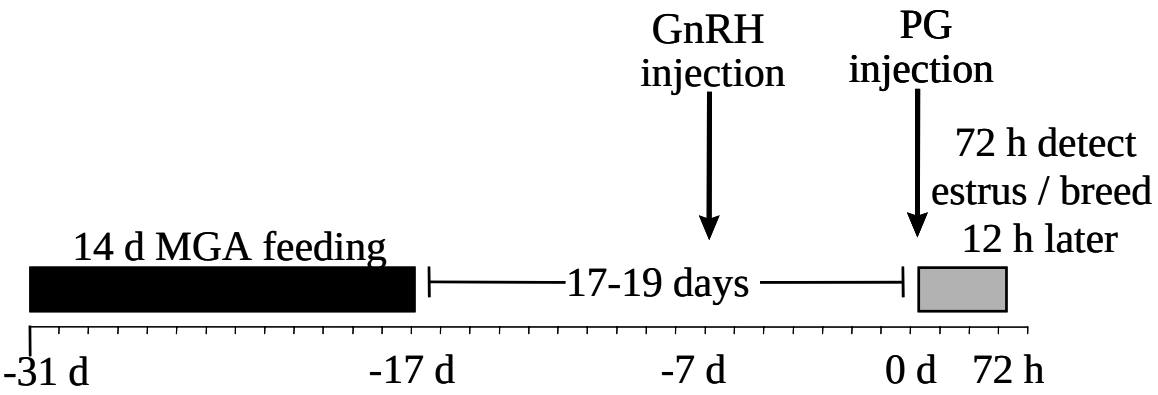

Figure 13. A modification of the MGA (progestogen)/PG (prostaglandin $F_{2\alpha}$) system utilizes an injection of Gonadotropin-releasing hormone (GnRH) 7 days prior to PG injection

Summary

Synchronization of fertile estrus in heifers can be accomplished with progestogens, combinations of progestogens and prostaglandin $F_{2\alpha}$, prostaglandin $F_{2\alpha}$ alone, and combinations of gonadotrophin-releasing hormone and prostaglandin $F_{2\alpha}$. Advantages and disadvantages of each system as well as the management capabilities and expectations of the producer should be considered when determining the most appropriate estrous synchronization product or protocol.

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