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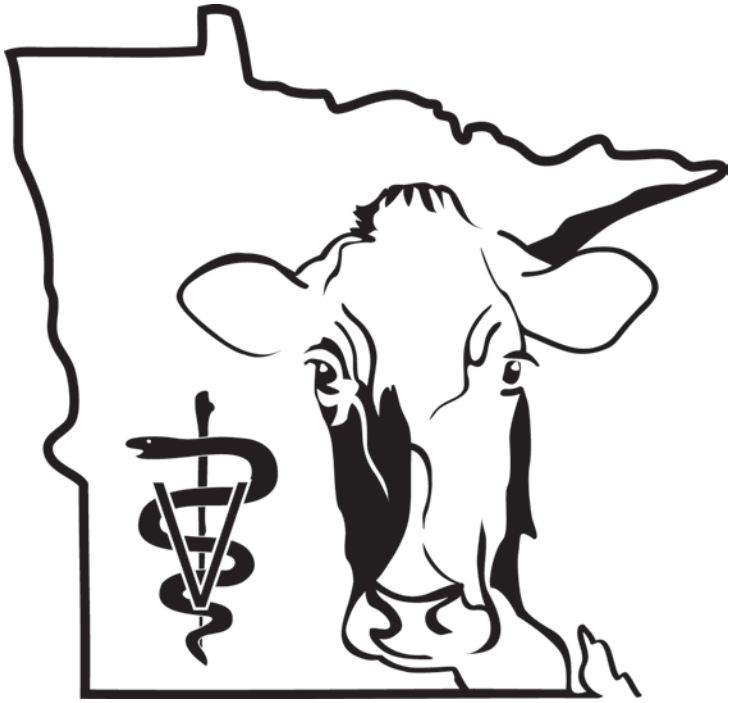

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Reproductive Physiology Affecting Controlled Breeding Programs

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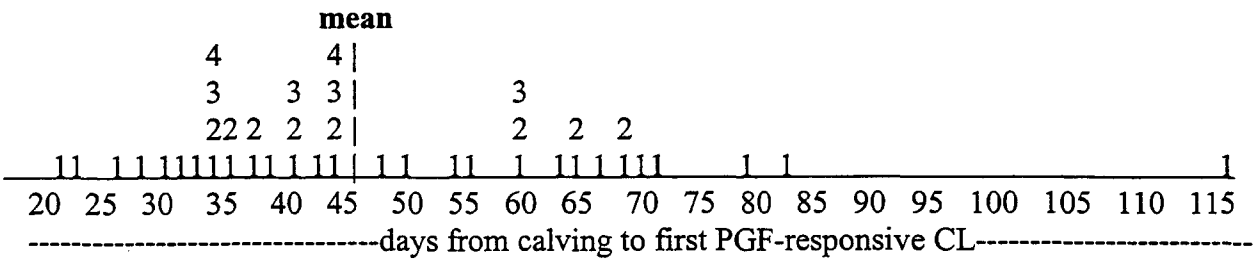
Basics of Estrus Control or Synchronization in Cattle

In cattle high progesterone (P_4) blocks the onset of estrus. The P_4 blocking estrus during the diestrous phase of the estrous cycle and during pregnancy comes from the ovarian corpus luteum (CL), while exogenous P_4 given as a feed supplement, an injection, an implant or via a vaginal suppository suppresses estrus until removed for estrus control. Estrus occurs in 2 to 4 days, depending on product, after the P_4 is removed. In bovine reproductive physiology, the nonpregnant uterus sends a signal to the ovary ending life of the CL. We can now use prostaglandin F2a (PGF) products to kill the CL and the return to cow to estrus in 3 to 4 days.

Terms such as "estrus induction" or "induced estrus" should be avoided in cattle, as available products and techniques are generally not able to induce or create a physiologic, fertile estrus in cows that are not having normal estrous cycles. True anestrus, that is not having the ovarian activity associated with normal estrous cycle patterns, is most commonly due to cows or heifers being 1) sick, 2) prepuberal, 3) postpartum, 4) under-conditioned or 5) pregnant.

Postpartum Considerations

1. How Long Does Postpartum Anestrus Last in Dairy Cows? Remember that only half the group can respond to PGF products at the average or mean interval to presence of the first CL and that for best results with estrus control programs all cows must be cycling at the start of treatment. A project in which we measured postpartum days to first significant rise in milk P_4 in dairy cows at the Southern Experiment Station Herd in Waseca, MN showed how averages can be deceiving in this situation. We found that 11 (26%) of 43 cows had not developed at PGF-responsive CL by day 60 even though the average interval to first CL_3 was 46.9 days (in the following table, see the variation in this measurement among the 43 cows). Note that one cow



did not develop a CL of any size until she had her first estrus and was bred (but did not settle) at 107 days postpartum. Milk production genetics were influential here as the average for 21 cows in the 1964 genetic control group which produce 13,000 to 14,000 pounds of milk per year was 42.1 days versus 51.5 days for 22 cows in the modern genetic group bred for highest possible

milk production which produce 23,000 to 24,000 pounds of milk per year. This was also the topic in a recent Artificial Breeding column by Dr. Jeff Stevenson in Hoard's Dairyman.[1] Major points made were that dairy herds may have 16% to >50% of their cows not cycling by day 60 after calving, that younger and thinner cows are more likely to not be cycling, and that early postpartum resumption of estrous cyclicity is highly correlated with higher dry matter intake.

More information is needed to determine reasonable standards for duration of ovarian inactivity, ie true anestrus, in today's newer dairy setups that tend to be major users of controlled breeding/appointment AI programs for first service; that is for cows in large freestall facilities milked 3X/day, on BST, and group fed a TMR. Ideally some method of determining or monitoring the postpartum interval to the first CL is needed on each of these larger operations.

For successful results, all controlled breeding programs available today depend on their being applied to cows that are having estrous cycles at the start of the estrus control regime. While some regimes may have mild stimulatory effects, there are no currently available treatment regimes using FDA-approved products that have consistent efficacy in initiating estrous cycle activity in noncycling cows.

Gonadotropin releasing hormone (GnRH) was reported many years ago to be 100% effective for inducing ovulation and the onset of estrous cyclicity in dairy cows at 14 days after calving.[2] However in 3 recent trials attempting to reproduce such results we have only been able to achieve ovulation and initiation of estrous cyclicity in 50% of 46 dairy cows although all but one cow responded to the GnRH with release of luteinizing hormone (LH).[3] Parity had a significant effect on ovulation response as only 1 of 13 primiparous versus 7 of 13 multiparous cows ovulated in response to a one-time GnRH treatment on day 14 postpartum. Only cows with a ≥12 mm follicle, as measured by ultrasonography, ovulated in response to the GnRH treatment.

2. Reproductive Performance of Normal vs Abnormal Dairy Cows: The following table from Stevenson and Call[4] presents data from one large dairy herd comparing reproductive results between herdmates with normal versus abnormal postpartum periods (problems were retained placenta, cystic ovaries, prolonged anestrus, twinning, metritis indicated by palpation findings or presence of a purulent discharge at the time of insemination). By these criteria nearly 30% of cows in this herd were classified as having had an abnormal periparturient experience. We recognize that cows with these conditions have problems at the time the condition is present but these results show that these problems have longer term effects that adversely affect subsequent rebreeding performance. Attempting to breed an increasing number of abnormal cows and a

Trait Measured	Normal Cows	Abnormal Cows
Number of cows	592 (71%)	242 (29%)
Aver days to 1st estrus	66	74*
Aver days to 1st AI	70	78*
Aver days open	98	131*
Services per conception	1.9	2.6*
Conception rate at 1st AI	44%	22%*
Pregnancy rate	91%	68%*

*Data in rows with this mark differ statistically at P<0.05 between normal and abnormal cows.

decreasing number of normal cows may be part of the reason for the marked decrease in reproductive performance of Minnesota dairy cattle in recent years.[5] For example, 1998 Minnesota DHI data shows an average conception rate of 34% and an average estrus detection rate of 35% which gives a pregnancy rate per 21-day estrous cycle of only 12%.[6]

3. How Many Cows Are Being Bred at Their First Ovulation Postpartum?: In a classic study of the effects of early postpartum breeding on AI results, Whitmore etal[7] found a strong correlation, as shown by the following table, between conception rate and the number of the estrous periods preceding first AI regardless of number of postpartum days to the first estrus.

Postpartum Estrus Number at First AI	Number of Cows Bred	Conception Rate
First	17	35%
Second	28	50%
Third	67	73%
Fourth	61	72%
Fifth	7	100%

These results suggest that the downward trend with conception rates in Minnesota DHI herds toady may be due to our breeding an increasing percent of cows at their first estrus after calving.

4. Guidelines to screen groups of cattle for the absence of an anestrous problem include:

a. 4% to 5% of a group should be in estrus each day and 50% to 60% should have a large CL by rectal palpation at any time before any synchronization treatment has occurred. To determine if a particular cow is cycling, palpate every 7 to 14 days until a large CL is found. Presence of a follicle does not prove that the cow is cycling nor that she is about to be in estrus. Many follicles regress without ovulating.

b. 50% to 60% should be seen in estrus on days 2 through 5 after a first PGF treatment.

c. nearly 100% should have a large CL by rectal palpation at the time of a second PGF treatment at 11 days for heifers to 14 days for dairy cows after a first PGF treatment.

When Should Controlled Breeding Programs Start Postpartum?

Good News: Days from the end of the VWP to AI will be shorter and under your control with an estrus control breeding program that uses appointment AI. So it is appropriate to reconsider the length of the postpartum voluntary waiting period (VWP). When designing estrus control plans for entire dairy herds, previously accepted reproductive standards and guidelines should be open for reevaluation. For example, it may not always be appropriate to continue using a short postpartum VWP since estrus detection failure will no longer be a factor in determining average days to first AI. Rather it may be better to plan the system, that is, postpartum starting dates, to meet specified goals. For example, it may be best to delay the start of breeding to coincide with the herd's desired average interval to first AI, as some of these programs are guaranteed to produce that figure as the herd's actual result. This change could (1) eliminate the excessively short lactations that occur with first-service conceptions in herds with short postpartum VWPs, (2) allow more cows to overcome postpartum anestrus by the time of the controlled breeding, and (3) increase first-service conception and pregnancy rates by allowing a longer time for postpartum uterine involution.

Bad News: Remember that the treatment time required to administer the estrus control program's treatments must be added to the postpartum anestrous interval when planning the voluntary waiting period (VWP) to first AI with these programs. For example, time from the start of the program to the resulting AI is 10 days for Ovsynch, 17 days for double PGF followed by time AI, and 35 days for Presynch (Presynch = Ovsynch preceded by double PGF to improve the ability of cows to respond by increasing chances of cows having a CL_3 when given the Ovsynch PGF treatment).

My personal choice is to lengthen the VWP when controlled breeding programs are used in dairy herds so that first services occur at 70 to 80 days for mature cows and about 20 days later for first calf heifers to maximize reproductive return on the investment being made.

What Do Prostaglandin Products Do? When During the Cow's Estrous Cycle Do They Have This Activity?

The following is the sequence of events that occur when cows with a mature CL are treated with PGF products:

1. P_4 output by the CL stops.
2. Blood P_4 decreases in 1 to 2 hrs to nearly undetectable in 24 hrs.
3. CL size decreases over 2 to 3 days.
4. Estrogen from developing follicle rises over 24 to 72 hrs.
5. Estrus begins about 72 hrs (range = 60 to 120 hrs).
6. LH surge occurs near the onset of estrus starting the ovulation process.
7. Standing estrus lasts 8 to 18 hrs.
8. Ovulation occurs 24 to 30 hrs after estrus onset.

No difference was found in the abilities of Estrumate and Lutalyse at standard approved doses to initiate the events listed above.[8] These events can be expected only when cattle that have a PGF-responsive CL are treated; that is, during the diestrous phase (days 7/8 through 18) of the estrous cycle. So PGF treatments given to dairy cows

between 0 and 5 days after estrus produce no response,
treatments on day 6 have only a 25% response,
treatments on day 7 have a 67% response and
thereafter treatments approach a 100% response.[9]

So, in order to get desired response rates, PGF treatment for lactating dairy cows needs to be delayed until days 7 or 8 after estrus or $\geq$7 days after post-estrual bloody discharge. The problem is recognition of this time in a clinic situation, given the variations of CL size, shape and growth rate in individual animals.

Heifers vs Cows: Table 3, which compares PGF effects in heifers to cows at two times during diestrus,[9] shows that heifers begin estrus sooner after PGF than cows, and that estrus occurs sooner and more predictably when PGF is given on days 7 to 9 of the estrous cycle than if given on days 10-13. These differences are caused by variables in follicular rather than CL effects. Note also in Table 3 that at day 7 dairy cows are less responsive (72%) than are dairy heifers (89%), indicating that CL growth can be slower in cows than heifers.

Table 3: Estrus Response Rate and Estrus Time Variability to Prostaglandin Treatment Affected By Type of Animal and Stage of Diestrus[9]

	-heifers-		--cows--	
	-----Day treated*-----			
	7	10	7	10
No. treated	27	24	25	23
Estrus rate (%)	89	100	72	96
Hrs to estrus	49	79	60	100
Stnd dev (+/-)	4	19	9	39

*Day of the estrous cycle relative to estrus (day of estrus = day 0).

Semen quality and AI technique:

Fertility among AI bulls varies but fertility disasters with semen from CSS certified studs are very rare. Semen may be damaged in transfer and/or storage after leaving the bullstud so it is best to purchase frozen semen directly from the primary producer.

Thaw temperature and time recommendations issued by the bullstud source of the semen being used must be closely followed for best results (usual thaw guidelines for semen frozen in 0.5 cc straws are to use 30-35 C water for 30-40 seconds). A recent study shows that the number of semen straws thawed at one time can affect conception rates.[10] When four straws were thawed and loaded at the same time by one technician, conception rate with the first straw used was 48% but only 25% for the fourth straw, with an elapsed time between the 1st and 4th AI of only 6 minutes. And this was done in Hawaii where environment temperature would not be the concern we would have here

Site of semen deposition is probably a highly variable component in the AI procedure since the onset of on-farm inseminators. For best results, it is critical that intrauterine deposit be achieved. In one study cervical deposition produced a 39% conception rate versus 49% for uterine body or uterine horn deposition.[11] Vaginal deposit of AI semen rarely produces a pregnancy! Local veterinarians are usually the first source of advice and help.

The Basic Estrus Control Programs

Prostaglandin F2 alpha (PGF) can be used in four basic plans to synchronize estrus in groups of cattle. Each has its characteristic advantages and disadvantages, and each has the potential to be used repetitively within the same breeding season or even all year around, for example, in dairy herds.

1. The classic method is **double PGF** with injections given 11 to 14 days apart (the shorter interval works better in heifers and the longer interval is better for lactating dairy cows), with AI after the second PGF injection based on (a) estrus detection, or (b) timed appointment at 72 to 80 hrs for cows and 60 to 68 hrs for heifers or (c) double-timed appointment about 72 and 96 hrs for cows and 60 and 80 hrs for heifers. The response expected of cows at each of the days of the 21-day estrous cycle to this plan is shown in Table 1. Reproductive results with this method, with AI once at 75 to 80 hrs (183 cows) or twice at 72 and 96 hrs (176 cows) after the second injection, were compared to a control using AI based on conventional estrus detection for

21 days (176 cows) on 2 farms.[12] Results showed no advantage for double AI in this system (46% vs. 47% conception rates), showed similar conception rates between controls and PGF groups (50% vs. 46% and 47%), and demonstrated the advantage an increased AI submission rate (61% vs. 100% and 100%) has on pregnancy rate (30% vs. 46% and 47%).

Table 1: Mechanism Of Action by which the Double-PGF Injection Plan (with 14 days between injections) Synchronizes Estrus in Groups of Cattle

Day of Estrous Cycle at 1st PGF--->	Status in 3 days		Day of Estrous Cycle at 2nd PGF ->	Status in 3 days	
day 1	day 4		day 15	**Estrus**	
day 2	day 5		day 16	**Estrus**	
day 3	day 6		day 17	**Estrus**	
day 4	day 7		day 18	**Estrus**	**Estrus**
day 5	day 8		day 19	**Estrus**	**rate**
day 6	**Estrus**/d9	**Estrus rate**	day 11	**Estrus**	**near**
7-->17	**Estrus**	**of**	day 11	**Estrus**	**100%**
day 18	**Estrus**	**55 to 60%**	day 11	**Estrus**	
day 19	day 1		day 12	**Estrus**	
day 20	day 2		day 13	**Estrus**	
Estrus	day 3		day 14	**Estrus**	

2. A modification of method 1 is a **one PGF for all, and two for some** program where one injection is given to the entire group with AI during the next 5 days for those seen in estrus, and then a second injection is given only to nonresponders in 11 to 14 days with AI based on estrus detection or timed appointment. This method lowers doses of PGF required and spreads the AI effort over more time. A 61% conception rate and a 58% pregnancy rate occurred with this plan in 985 dairy heifers from several farms.[13]

3. Another approach is **PGF for selected cows** where ovarian palpation or milk P_4 is used to detect cows that have a PGF-responsive CL for a single PGF injection, with AI based on estrus detection or by timed appointment. It is best to use double-appointment AI at about 72 and 96 hrs for cows or 60 and 80 hrs for heifers when preceded by only one PGF injection. This method can be used once per group or repeated at one or more intervals of 7 to 14 days to get a greater portion of the group inseminated.

When Howard (personal communication) used this method on beef cows, the conception rate was 36% (172 cows) with one timed AI at 72 to 86 hrs vs. 49% (185 cows) with two timed AIs at 72 and 96 hrs. In another trial, this plan was compared to conventional estrus detection and AI in three dairy herds in stanchion barns using 99 breedable heifers (48 in the PGF system and 51 controls) and 447 cows (219 in the PGF system and 228 controls).[14] In the PGF system, a veterinary visit occurred the same day each week for palpation of cows and heifers ready for breeding and PGF was given when a mature CL was found. AI was based on once-daily AM estrus detection. The program was conducted in three consecutive fall-through-spring breeding seasons. The PGF system improved days to first AI (by 13 days for heifers and 11 days for

cows) and to conception (by 18 days for both heifers and cows) relative to controls. The 267 animals in the PGF system were treated with 313 doses of PGF; and 88% of first AIs and 82% of all AIs in the PGF system occurred on days 2 through 5 after the day of the veterinarian's visit and PGF treatment; and conception rate for AIs 2 to 5 days after PGF was higher than that at all other AIs in the study (58% vs. 47%).

4. Another popular way to get started with PGF estrus synchronization in a more gradual manner is a **12 day program** where AI based on estrus detection starts for a group of cattle without PGF treatment, then PGF is given on day 7 to all cattle not yet inseminated and AI continues for 5 more days. This method uses the fewest doses of PGF per animal bred and the first 6 days allows a good monitoring period of the group's cyclicity status before PGF is given (see General Guidelines for anestrus later in this section), but the AI effort is spread over 12 days.

In another field trial, this plan was applied to 52 beef cows with suckling calves 51 to 87 days old on the first day of breeding.[15] Twenty cows were in estrus and bred prior to PGF and 28 of 32 were in estrus and bred after PGF injection. Day 3 after PGF was the busiest day with 18 cows (35% of the group) bred. Prior to PGF, the average daily estrus rate was 6.4% (see later General Guidelines for anestrus) indicating little or no anestrus in this group. The conception rate was 65%, the pregnancy rate was 60% and services per conception was 1.7 (four cows were bred twice). Conception rates before PGF (60%) and after PGF (68%) did not differ.

Combination Approaches for Estrus Synchronization of Groups of Cattle:

1. Exogenous P_4 products plus CL termination (by estradiol or PGF injection) can be used to shorten the required duration of P_4 exposure to 9 or 10 days, which seems to be key to achieving normal fertility at the synchronized estrus. **Syncro-Mate-B or SMB** (Rhone Merieux, Athens, GA) and **Melengestrol Acetate or MGA** (Pharmacia Upjohn, Kalamazoo, MI) are the only P_4 products of this type approved for cattle use in the United States.

Examples of P_4 plus PGF or Estrogen Combinations:

SMB has Food and Drug Administration (FDA) approval as an estrus control agent for beef cattle and dairy heifers but not lactating dairy cows. The SMB treatment consists of an ear implant (6 mg norgestomet) and an IM injection (3 mg norgestomet and 5 mg estradiol valerate). The ear implant is removed after 9 days and AI is based on observed estrus usually beginning in about 36 hours or is by appointment 48 to 54 hours after implant removal.

In the same field trial cited above[15], another group of 54 beef cows with suckling calves 51 to 87 days old were treated with SMB and then bred based on estrus detection. The conception rate was 65%, the pregnancy rate was 57% and services per conception was 1.7 (5 cows bred twice in the 5 days after implant removal). The busiest breeding day was day 2 after implant removal when 42 cows (78% of the group) were bred. In another SMB trial, 79 control heifers were bred by AI based on estrus detection for 25 days vs. 79 SMB-treated heifers bred based on estrus detection vs. 80 SMB-treated heifers bred by timed AI at 48 hours.[16] Respectively, estrus or AI submission rates were 94%, 84% and 100%; conception rates were 72%, 73% and 55%; and pregnancy rates were 67%, 61% and 55%. The conception rate was lower for SMB-treated heifers bred by timed AI but the pregnancy rate was not different among treatments. Seguin et al.[17] compared the classic PGF system (double PGF 11 days apart with timed AI at 60 to 62 hours after the second PGF) and the SMB system (timed AI at 48 to 50 hours after implant

removal) in 7 groups of beef or dairy heifers. Results in 5 cycling groups were 41 (53%) of 77 heifers pregnant with the PGF system and 34 (45%) of 75 heifers pregnant after the SMB system, but in two groups of anestrus heifers only 6 (18%) of 34 heifers were pregnant after PGF and only 7 (21%) of 33 heifers were pregnant after SMB. So these PGF and SMB systems were equally effective for cyclic heifers and equally ineffective for anestrus heifers.

A **controlled intravaginal drug-releasing device (CIDR)** and a **progesterone-releasing intravaginal device (PRID)** are available in other countries to deliver P_4 via a pessary. The injection used with these products can be estrogen if given at the beginning of the P_4 treatment period or it can be PGF if given at or near the end of the P_4 treatment. The only option in these programs is deciding whether AI will be based on estrus detection or timed appointment. The CIDR and PRID have been studied as a way to synchronize second service in cows not pregnant to the first AI by reinserting them 10 days after a first AI and then removing them 9 days later, without PGF or estrogen injection, with all second services based on estrus detection.

MGA followed by PGF has been used only in heifers due to its long treatment time (30 to 32 days). MGA is fed at 0.5 mg/head/day for 14 days and PGF is given 16 to 18 days after the end of MGA feeding. Although many heifers show estrus after withdrawal of MGA, breeding is delayed until after PGF to maximize fertility. This system requires that heifers are fed some concentrate or total mixed ration in which the MGA can be mixed to assure that each heifer gets the required MGA each day. In one trial, this method was compared with SMB with AI based on estrus detection in 310 yearling beef heifers. The MGA followed by PGF method produced higher conception (69% vs. 41%) and pregnancy (57% vs. 37%) rates.[18]

Another beef and dairy heifer trial compared an **MGA plus PGF** combination which is MGA fed at 0.5 mg/day for 7 days with PGF given on day 7 to untreated control and 1X-PGF groups.[19] Respective conception rates in 6 days of breeding were 51%, 59%, and 68% while respective pregnancy rates in 6 days were 39%, 16%, and 37% but pregnancy rates did not differ among groups after 24, 30, or 60 days of breeding.

2. CL termination via PGF products plus control of follicular cycles via gonadotropin releasing hormone (GnRH) has been looked at in a variety of combinations for controlled breeding of cattle. Of these a system called **Ovsynch** has been the most widely used.[20,21,22] Here each cow gets three injections: injection #1 is GnRH on day 1 to synchronize growth of a new wave of follicles and to assure presence on day 8 of a CL (needed to keep cows from coming into estrus before the next injection and to make them PGF responsive), injection #2 is PGF on day 8 to regress all CL's (hopefully now present in every cow), which will allow or cause the new dominant follicle to proceed toward maturation, and injection #3 is GnRH on day 10, about 48 hours after PGF, to trigger ovulation. AI occurs on day 11, about 16 to 24 hours after GnRH. [Note: Some of the time intervals are still being studied and could change in the future.] Variations of the Ovsynch program include Select-Synch and Pre-Synch. Select-Synch is the same as Ovsynch with the exception that the second GnRH is not used and AI is based on estrus detection. This variation has been popular for beef cattle, but has also been used on dairy farms that prefer AI based on estrus detection over timed AI. Pre-Synch is the addition of another PGF treatment 14 days before the first GnRH treatment. The possibility of substituting human chorionic gonadotropin (HCG) for GnRH in the Ovsynch protocol was studied but HCG results

were not equal to those with GnRH.[23,24] In another possible PGF/GnRH combination program, no advantage was found to giving a GnRH injection on day 7 in a double PGF treatment 14 days apart.[25]

ESTRUS CONTROL or SYNCHRONIZATION on the FARM

For Individual Cows:

Failure to observe estrus within 21 days after the postpartum voluntary waiting period (VWP) or after service in cows which have not conceived has been the major negative influence on reproductive performance in conventionally managed dairy herds. Zemjanis et al.[26] reported that anestrus occurred at 43% of expected estrous periods in dairy cows. However true anestrus (failure of cows to have estrous periods) accounted for only 10% of this incidence, with the remaining 90% due to failure of cycling cows to be seen when in estrus. Thus Zemjanis et al. entitled their article "Anestrus: The Practitioner's Dilemma" in recognition that man's role in estrus detection was a greater problem than were conditions directly preventing ovarian function and estrus behavior in cows. True anestrus caused by ovarian atrophy can be a problem in individual cows that have complications at calving and on a herd basis where nutritional deficiencies and lack of body condition exist. Therapy for this problem is rarely successful so the condition is best prevented through management changes.

Since most dairy cows presented to veterinarians for anestrus are having estrous cycles but not being observed in estrus, the condition is more accurately named **unobserved estrus**. Palpation of these cows finds about 55% in diestrus with a functional CL (a smooth plump protruding structure with liver-like consistency about 2.0 to 2.5 cm in height and diameter that greatly alters the ovary's size and shape), 15% in proestrus 1 to 3 days before estrus, 5% in estrus and 25% in metestrus 1 to 6 days after estrus. Two clinical approaches for these cattle are (1) prediction of estrus based on palpation findings and (2) PGF for estrus control in diestrus cows.

The literature on field results using PGF products in dairy cows shows that, in most cases, about 65% of clinical cases of unobserved estrus treated with PGF products are observed in estrus and inseminated as a result of PGF treatment.[27] Why this relatively disappointing result? Three factors are involved: (1) absence of a PGF-responsive CL in treated cows, (2) estrus detection failure after PGF treatment, and (3) perhaps stress related to production, heat or social interaction among herdmates depressing behavioral expression of estrus. Combining the estrus response from two of our field studies[8,27], distribution of observed estrus in 280 dairy cows responding to PGF treatment for unobserved estrus was: day 1, 2%; day 2, 8%; day 3, 38%; day 4, 32%; day 5, 14%; and day 6, 6%. This spread can destroy a farm's enthusiasm for estrus detection efforts needed to maximize PGF results. Even in Minnesota, season can affect PGF results. On one farm, observed estrus rate was 66% for 32 summer treatments vs. 80% for 40 winter treatments, and resulting conception rates were 30% in summer vs. 52% in winter for a pregnancy rate as a direct result of PGF of 20% in summer vs. 42% in winter.

Recommendations for the AI Plan in Unobserved Estrus Cows Treated with PGF

Most veterinarians and dairy farmers seem to prefer AI based solely on estrus detection after one-time PGF treatment in dairy cows for unobserved estrus. This is most appropriate in view of the

three factors just discussed regarding apparent estrus response after PGF treatments and the relative costs of PGF versus semen. Concerted estrus detection efforts two to three times per day are encouraged at all times but especially during periods of expected estrus response to PGF, and AI should mainly be restricted to those cows showing strong signs of standing estrus. As a secondary recommendation (but one that may be most appropriate on some farms), appointment AI may be considered. The advantage and/or disadvantage with appointment AI is that all treated cows get inseminated. Lactating dairy cows should be inseminated about 72 and 96 hours after PGF and heifers about 12 hours earlier because double-appointment AI has produced a significantly higher pregnancy rate (59%)[27] than is likely with a single-appointment AI in this single PGF injection situation.

Another consideration on this point is that when appointment AI is used, veterinarians will feel more pressure for very accurate selection of cows for PGF treatment because every animal treated gets inseminated. Other disadvantages are that more semen is needed and that some cows, up to 20%, will show estrus after the last-appointment AI and therefore require even a third AI.

Economics of PGF Use in Unobserved Estrus Dairy Cows:

Using computer modeling techniques, AI by detected estrus was more profitable than appointment AI at nearly all input assumptions.[28] The exceptions were if estrus detection rate was poor (<40%), cost of semen was low (<$5/dose) or CL diagnosis was very accurate (>90%).

How Accurate Can We Expect to be with CL_3 Identification by Rectal Palpation?

Many of us feel that we can select with very high accuracy cows by rectal palpation for a CL_3 that will respond to PGF treatment, and yet this has become a controversial topic as some popular press articles have stated that veterinarians are not very accurate with this procedure. However we know in the real world that not all cows given PGF are seen in estrus as expected 3 to 5 days after treatment. While we know that PGF products approach 100% efficacy in the ability to kill the diestrual CL, that is in cows 8 through 18 days after their last estrus; in the summation of most field use of PGF to treat cows for unobserved estrus based on rectal selection for a PGF-responsive CL, only about 65% are observed in estrus and inseminated within the expected response time.[11] How much of this failure is due to erroneous selection of cows to be treated? While there have been trials in which the selection of cows for PGF treatment was very accurate, e.i. over 92% of cows selected of treatment had >2.0 ng of P_4/ml of blood plasma;[29] there have been other field trials where selection accuracy by this criterion was closer to 75%.[30] There are two sides to the question of palpation selection of cows for PGF treatment; one is the accuracy of including cows for treatment and the other is the accuracy of excluding cows from treatment. Ott and colleagues concluded from their own trial plus the review of data from three other reports that palpation errors were made by the inclusion of 18% of 244 cows for PGF treatments that did not have diestrual CLs and by the exclusion of 30% of 158 cows from PGF treatments that had diestrual CLs.[30] There are some things about this report that can be questioned. It is now known that P_4 results are more accurate when samples are analyzed as blood plasma rather than blood serum.[31,32] Also their gold standard of >1.0 ng/ml of P_4 as the indicator of which cows can respond to PGF is not perfect since many cows will have >1.0 ng/ml of P_4 well before they reach day 8 after estrus which is the first day when more than 90% of dairy cows can respond to PGF.[12]

For Herd Reproductive Management:

This discussion will be restricted to PGF since that is the only estrus synchronization product approved in the United States for use in dairy cows, but in some other countries the CIDR and PRID can be used in lactating dairy cows.

Why Consider Dairy Herd Estrus Control Programs? These systems can:

1. replace estrus detection 2-3 times of every day that is ineffective on many farms.
2. eliminate estrus detection and AI from some days of each week or from some weeks of each month. This can change labor needs and improve herd performance by making reproductive management a major task on fewer but preplanned days, rather than one of many jobs to be done every day.
3. improve herd reproductive performance by:
   a) increasing chances of >1 cow being in estrus at a time, which will create groups of sexually active cows and make estrus detection easier.[33]
   b) raising estrus detection rate from the industry average of about 45 to 50%.
   c) decreasing average days in milk at first AI and days open without lowering the herd's VWP (see paragraph 1 under "Considerations" later in this article).
   d) focusing attention on pregnancy rate per estrous cycle (% pregnant every 21 days of those ready for breeding) rather than on conception rate data which has less relative importance.

Monday (or Friday or ???) Morning Program

Seguin et al.[14] initially tested a single PGF injection scheme with palpation selection every 7 days for cows with PGF-responsive CL and saw improved reproductive performance concurrent with evidence of decreased labor for estrus detection. One Wisconsin veterinary practice promoted a variation of this scheme, in which a veterinarian visits the farm every 14 days to perform palpations of cows ready to be bred and, if a CL is found, PGF treatment is given.[34] All first AIs must be preceded by a PGF treatment, and AI based on standing estrus is stressed. This allows estrus detection efforts to be focused on a 4-day period every 14 days although 21-day repeats would not fall during this 4- day window. Improved herd reproductive performance, reduced labor, increased income (+$76 [1985 dollars] per cow per year) and client satisfaction were reported with this program. This practice expects 60% to 70% of PGF treatments to produce a strong estrus and AI. If estrus response falls below 50% despite good estrus detection effort, nutritional problems are suspected and feed analysis and ration balancing are recommended. On the other hand, estrus response rates that are very high (near 100%) may indicate that cows are being inseminated just because they were treated, rather than because strong signs of estrus were seen, and that will lower the conception and pregnancy rates.

These "Monday Morning" programs can also be run without palpation selection of cows for PGF treatment by injecting all cows ready for breeding that have not yet been inseminated or that are known to be open after breeding.[35,43]

Target Breeding Program

The **Target Breeding Program** is essentially the 14-day plan discussed above[34], with two

changes: (1) each cow gets a PGF injection before she is ready for AI to "set-up" her estrous cycle to increase her chances of being in diestrus 14 days later when she is ready for breeding and given a second PGF treatment; and (2) palpation selection for PGF responsiveness is not usually used.[36] One day in each 2-week interval is selected that will be convenient for PGF injections and for optimal estrus detection 3 to 6 days later. To start, cows in the last 14 days of their VWP (not necessarily the same for all cows or all groups of cows; for example, first-lactation heifers vs. older cows) are given the initial set-up PGF injection. Each cow then gets a second PGF injection 14 days later (so called "breeding shot"), followed by maximized estrus detection effort and AI. A goal is for at least 70% of these second PGF injections to produce an observed estrus. At the same time, the next cows ready for breeding (group 2) are given their set-up injection. In another 14 days, group 1 cows not yet inseminated get a third PGF injection, group 2 cows get their first breeding shot and group 3 cows get their set-up shot. This continues every 14 days as long as there are cows to be bred. Appointment AI may be used after the second or third PGF breeding injection. One Pennsylvania herd in the Target Breeding Program for 2 years increased their pregnancy rate at 120 days postpartum from 60% to 80%. More evaluations of this program in controlled research situations are needed, however.

Two possible shortcomings should be understood by potential users. One is that noncycling cows will not respond in this system and to the extent that true ovarian inactivity or anestrus exists as a herd problem at PGF injection times, the program will fail to meet expectations. Another point is that although the first impression may be that this program will allow farms to decrease estrus detection efforts to one 4-day window every 14 days, cows returning to estrus about 21 days after a "controlled" breeding will be outside this observation window.

Ovsynch Program

Ovsynch is a relatively new idea in bovine estrus control designed to synchronize ovulation, rather than estrus, and allow AI without estrus detection.[20] In the Ovsynch program, each cow gets three injections. Injection #1 is gonadotropin releasing hormone (GnRH) on day 1, injection #2 is PGF on day 8 to regress all CL's (hopefully now present in every cow), and injection #3 is GnRH on day 10, about 48 hours after PGF, to trigger ovulation. AI occurs on day 11, about 16 to 20 hours after GnRH. [Note: Some of the time intervals are still being studied and could change in the future.]

Ovsynch emphasizes pregnancy rate results, rather than conception rate results, as the way to improve overall herd reproductive efficiency. This program raises the estrus detection rate (better named the AI submission rate here) to 100% by relying totally on timed breeding, while hoping to maintain reasonable conception rates. To illustrate, note the theoretical calculations in Table 2. It is apparent by this example that some sacrifice in conception rate in exchange for a 100% estrus detection or AI submission rate can be worthwhile. Pregnancy rates with Ovsynch in lactating dairy cows were equal to those of control cows that were bred based on estrus detection after PGF (38%, n=156 vs. 39%, n=154) but were much lower in Ovsynch-treated dairy heifers than in control heifers bred based on estrus detection after PGF (35%, n=77 vs 74%, n=78).[14] Therefore, this program is not currently recommended for heifers. The program's effect on reproductive end points has been further tested in three herds of 333 dairy cows.[21] Relative to controls, Ovsynch cows had fewer days to first AI (54 vs. 83) and fewer days open (99 vs. 118), and more Ovsynch cows were pregnant at 60 days (37% vs. 5%) and 100 days (53% vs. 35%)

Table 2: Estrus Detection Rate, Conception Rate and Pregnancy Rate For Actual Minnesota DHI Data versus Theoretical Data with Estrus Control and Appointment AI in Dairy Herds

Reproductive Indices	Estrus Detection and AI	Estrus Control & Appt AI
1. Estrus detection or AI submission rate	43%*	100%
2. Conception rate	52%*	35%
3. Pregnancy rate for 1 cycle (#1 X #2)	22%	35%

*1994 Minnesota Dairy Herd Improvement Association (DHIA) averages.

after calving. Other Ovsynch trials have also reported conception and pregnancy rates near 30%.[37,38,39] A Minnesota grazier dairy used Ovsynch on one group of 54 cows and 36 heifers, with somewhat poorer results-although it happened that the AI day was the hottest day of the summer! The pregnancy rate was 19% in cows and 28% in the heifers treated and bred according to the plan (9 pregnant of 48 cows and 10 pregnant of 36 heifers), but 4 of the remaining 6 Ovsynch cows became pregnant when bred 24 hours early based on signs of estrus for an overall pregnancy rate of 26% (23 pregnant of 90 total females). Another farm used Ovsynch on 24 cows, with a pregnancy rate of 25% (6 pregnant of 24 cows). However others using Ovsynch in lactating Holstein cows have reported higher conception/pregnancy rates of 49%[40], 47%[41], and 44%[42].

Users of the Ovsynch protocol must be aware that the second GnRH injection has the effect of cutting short full development of behavioral signs of estrus so AI should be based on appointment timing rather than on detection of estrus. Ovsynch can be modified into an AI system based on estrus detection called Select-Synch by using only the first two injections (GnRH on day 1 and PGF on day 8) of the usual three injection Ovsynch scheme.

The standard dose of GnRH for cattle is 100ug IM but a recent report shows that the GnRH dose in Ovsynch can be reduced by 50% to 50ug IM without decreasing pregnancy rate results.[43]

Another important point from this paper is the rate of early embryonic death (EED) that occurs in cattle and the effect that early pregnancy diagnosis, for example by day 28 as is possible with ultrasonography, can have. In this study pregnancy rate at day 28 after AI was 41% but on day 56 after AI it was reduced to 34%. It was not determined here if EED was increased due to the early diagnosis of pregnancy or due to the Ovsynch breeding protocol. Another point of interest about the Ovsynch program, and all programs of estrous synchronization, is its relative effectiveness at each stage of the estrous cycle. This is especially critical with Ovsynch because it is a single PGF injection program, and a single PGF injection program will only control about 60% of a randomly cycling group (see Table 1). In our Ovsynch study[42] conception rate was highly dependent on cows having a functional CL at the time of PGF treatment; conception rate was 59% for 32 cows with high P_4 but only 13% for 16 cows with low P_4 (these 16 cows were cycling based on high P_4 at other times) . The P_4 data at each stage of the Ovsynch treatment raised questions about the ability of the GnRH treatment used to cause presence of a functional CL at the time of the PGF treatment. This apparent failure of Ovsynch to work at all stages of the estrous cycle may be due to the fact that the GnRH products now marketed in the USA (Cystorelin and Factrel) do not prolong CL activity[44] as has been demonstrated for a longer acting GnRH agonist known as buserelin.[45,46]

Basic Methods 1 and 4 Applied to Dairy Herds

In addition to the Monday Morning, Target, and Ovsynch programs discussed above, basic PGF methods 1 and 4, described earlier in this paper also have potential for dairy herds and have been simulation[47] and field[48] tested. In the field test a system using a double PGF treatment 14 days apart followed by appointment AI at 72 hours for first AI with all repeat AI based on estrus detection produced superior reproductive performance relative to controls and two other PGF reproductive management schemes.

Can We Plan on Dairy Cows Having 21-Day Estrous Cycles?

Some controlled breeding programs have been designed to eliminate estrous detection and AI from some days of each week or of each 21-day cycle,[48] under the assumption that the 21-day duration of the bovine estrous cycle is fairly predictable. But is that true? What is the length of the estrous cycle in cows which return to estrus after AI?

Jack Britt has presented data comparing estrous cycle lengths in lactating Holstein and Jersey cows before (n = 481 cycles) or after (n = 136 cycles) insemination.[49] As expected median and mode estrous cycle lengths were both 21 days for postpartum cycles before breeding (excluding the first estrous cycle after calving where 25% of cycles were less than 15 days long) and were both 22 days for estrous cycles after AI. The percent of estrous cycles 20 to 23 days long were 60.9% pre-breeding and 53.7% post-breeding but 28% of post-breeding estrous cycles were 25 or more days in length versus only 11% of pre-breeding cycles. So there is evidence of more variability in estrous cycle length, especially following a breeding, than would be desired to be relatively sure that most repeats would occur in given window of time after controlled breedings. This variability is likely to be increased where appointment AI is used, so that some cows may not be in estrus on the day of breeding.

III. Seasonally-Bred Herds:

A cow's **reproductive cycle or calving interval (CI)** is all reproductive events from one calving to the next. The reproductive cycle or CI has two parts: (1) the gestation period which is fixed at about 280 days PLUS the time from calving to next conception, i.e. days open. Days open also has two parts: (1) time for uterine recovery and resumption of regular estrous cycles. [This period is 45 to 60 days long for most beef and dairy situations but can be extended by problems.] PLUS (2) time for needed for rebreeding (estrus detection rate X conception rate/estrous cycle). **A yearly reproductive cycle or calving interval allows only 85 open days !**

The O'Connor System for Reproductive Management in Seasonal Beef or Dairy Herds

The goal of this program by the late Dr. Jim Wiltbank is more profit by optimizing the calf crop and the percent of calves born in the first 20 days of the calving season.[50,51] A 5-year transition will be needed to fully adopt this program.

Major points of the O'Connor Management System are:

1. Plan to cull and replace 15% of cows each year.
2. Replace late calving cows with early calving heifers.
3. Feed replacement heifers to start breeding 21 days before the cow herd.

4. Expose twice as many heifers to breeding as will be needed as replacements.
5. Select replacements from those that become pregnant first during a 42-day breeding season.
6. Maintain first-calf heifers separate from older cows and on a higher level of nutrition through their second breeding season while raising their first calves.
7. In the last 3 months of pregnancy, feed cows to a body condition score of 6 at calving. Some of this condition will be lost during the postpartum period, but cows should have a body condition score of 5 and gaining slightly at the beginning of the breeding season for best conception rates.
8. Be prepared to flush cows starting 3 weeks before breeding and to remove calves for 48 hours at the beginning of breeding. This can help increase the cycling rate in body condition score 4 cows or in better condition cows with short postpartum intervals.
9. Use breeding bulls that pass the BSE test within 30 days of the breeding season, and observe bulls for successful mating ability during the breeding season.

A **single injection of a PGF product on day 1 of (or 1 or 2 days before) the breeding season** to all cows ready for breeding could be component of the O'Connor program. In a three-year field study, this PGF treatment increased the number of cows served the first 4 days of the breeding season and cows calving in the first 10, 20 and 30 days of the calving season.[52] The PGF treatment caused 65% of cows fresh more than 30 days at the start of the breeding program to be served in the first 4 days of the breeding season, but it had little if any effect on cows fresh less than 30 days. Three-year old bulls that passed a breeding soundness exam each year were used in this study at a bull:cow ratio of 1:25. Average weaning weight increased by 13 pounds per calf as a result of earlier breeding caused by PGF treatment.

General Guidelines for Success

All estrus synchronization applications known today require that cows are having normal estrous cycles to respond successfully. Cows not having normal estrous cycles are said to be "anestrus". Causes include nutritional deficiency (especially energy), inadequate age (less than normal onset of puberty), inadequate VWP and the effect of calf nursing (beef cows with nursing calves seldom resume estrous cyclicity before 50 to 60 days after calving, even with the best management, herd health and nutrition) and debilitating disease or injury. Guidelines to screen groups of cattle for anestrus are as follows:
1. Before any estrus synchronization treatment has occurred, 4% to 5% of a group should be in estrus each day, and 50% to 60% are expected to have a large CL by rectal palpation at any time.
2. After a first PGF treatment, 50% to 60% should be seen in estrus on days 2 through 5.
3. At the time of a second PGF treatment (11 to 14 days after a first PGF), nearly 100% are expected to have large CL by rectal palpation.

Other management requirements necessary for a successful estrus synchronization and AI effort include:
1. Good facilities so cattle can be sorted and individually handled, injected, palpated, inseminated, and so on.
2. An individual identification (ID) system for each animal that is easily read from a distance.
3. A record system for each animal's reproductive (birthdate, parentage, breeding dates and service sire, calving dates, offspring ID, synchronization treatment dates, etc) and health (vaccinations, parasite control, etc) events.

4. Excellent technical services such as ovarian palpation for CL detection (if required in the synchronization program used), semen handling and intrauterine placement, and pregnancy diagnosis.

5. **Do pregnancy diagnosis as early as possible.** In all these ongoing PGF programs for reproductive management of dairy herds, identifying nonpregnant cows as soon as possible following AI, so they go back into the next new injection group and get rebred as soon as possible, is important for overall success. Ultrasonography can have an advantage over regular palpation.

6. **What interval between starting new groups of cows?** Most dairy herds, except graziers, breed throughout the year so the programs just described must be used repetitiously to incorporate new cows as they complete their VWP and previously bred cows found to be nonpregnant. Although many farms seem to opt for starting new groups every 14 days, consideration should be given to a 7- or 21-day interval between groups. Since cows have 21-day estrous cycles, either 7- or 21-day intervals between starting groups on these estrus control programs has the advantage that estrus activity from the new round of program treatments will coincide with the time when many of the nonpregnant cows bred on the previous treatment cycle will be returning to estrus. This is not the case if the interval between starting new groups is 14 days. In larger herds, starting new groups at 7 day intervals can have the same advantage over the 14 day interval and will reduce treatment groups to more manageable sizes.

Calving Patterns After Synchronized Breeding

It is commonly asked, when estrus control procedures for groups of cattle are talked about, if cattle conceiving on one day will all calve on the same day? The answer is NO! In groups of 100 beef heifers, 229 Angus cows and 105 Hereford cows that conceived on one day of synchronized breeding, calvings were spread over 21 to 23 days, with 9 (= 9% of group), 34 (= 14.8% of group), and 12 (=11% of group) calves born on the busiest day.

Precaution! These estrus synchronization products, especially PGF, will cause pregnant animals to abort, so this possibility must be considered before estrous synchronization is started. The health of females more than 100 days pregnant when treated with these products is a special concern in that these animals may not be able to completely abort the calf and therefore develop serious, if not fatal, metritis and septicemia.

Which is the best program? Each has advantages and disadvantages, none is clearly best for all situations. One of the strengths of estrus control methods in cattle today is the variety of options available. However some have been put off by this selection opportunity, apparently preferring to accept or reject a single cookbook recipe approach. The problem being that to take full advantage of one's options requires that decisions be made--hopefully from an informed point of view, which means most people will need to do some homework to fully understand and utilize these programs!

Estrus control programs have no magic!

Remember that larger groups of cattle are made of individual cows. We sometimes forget that all necessary reproductive physiology principles and management factors must work on an individual cow basis to have success on a group basis. There is no magic in larger numbers!

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