

Management Strategies to Improve Fertility in Lactating Dairy Cows

Paul M. Fricke and Ryan A. Sterry
Department of Dairy Science
University of Wisconsin-Madison

Implementing a Systematic Synchronization Program

Since pregnancy risk (**PRI**) is a function of both service risk (**SRI**) and conception risk (**CRI**), any attempt to improve PRI must consider both SRI and CRI. Service risk can be easily manipulated with the implementation of estrus or ovulation synchronization protocols, but CRI is, in most circumstances, more difficult to improve. Research in our laboratory at the University of Wisconsin – Madison has recently focused on systematic synchronization and resynchronization (**Resynch**) systems for lactating dairy cows as well as methods for increasing CRI and/or decreasing pregnancy loss (**PL**) after timed artificial insemination (**TAI**).

Implementation of a systematic synchronization protocol on a dairy can be achieved by answering two questions: 1) How will cows be submitted for first postpartum AI service? and 2) How will cows that fail to conceive to first service be re-enrolled for second and subsequent services? Examples showing data from farms in Wisconsin are presented to visually represent three representative ways that farms are approaching these management decisions.

Figure 1 illustrates the inefficiency of estrus detection for submitting cows to first AI service for a 500-cow herd managed using primarily visual detection of estrus for first postpartum AI service. Only ~10 % of cows in this herd receive first insemination

after a TAI. Days in milk (**DIM**) at first breeding is plotted on the vertical axis (y-axis) and date of freshening (i.e., time) is plotted on the horizontal axis (x-axis). Each square represents an observation, or a cow within the herd, and a bold line has been drawn horizontally at 100 DIM. Cows receiving first AI service before 100 DIM fall below the bold line; whereas cows receiving first AI service after 100 DIM fall above the bold line. Nearly one-third of the cows in the herd shown in Figure 1 exceed 100 DIM before first AI service. It should be obvious that none of these cows has a chance of becoming pregnant before 100 DIM because they have not yet been inseminated.

Although most dairy producers identify a set duration for their voluntary waiting period (**VWP**), breeding decisions for individual cows often occur before the VWP elapses. The VWP for the farm illustrated in Figure 1 is 50 DIM; however, many cows are submitted for AI before this time. The decision to AI a cow for the first time postpartum is determined based on when (or if) a cow is detected in estrus rather than on a predetermined management decision. In such instances, the cow is managing the decision to breed rather than the dairy manager. The decision to inseminate a cow before the VWP elapses is motivated by one factor, and that factor is fear. Most producers fear the decision to not breed a cow detected in estrus because she may not be detected in estrus again until much later in lactation. Unfortunately, this risk is often realized on dairies that rely on

Distribution of DIM at 1st AI Service: Farm 1

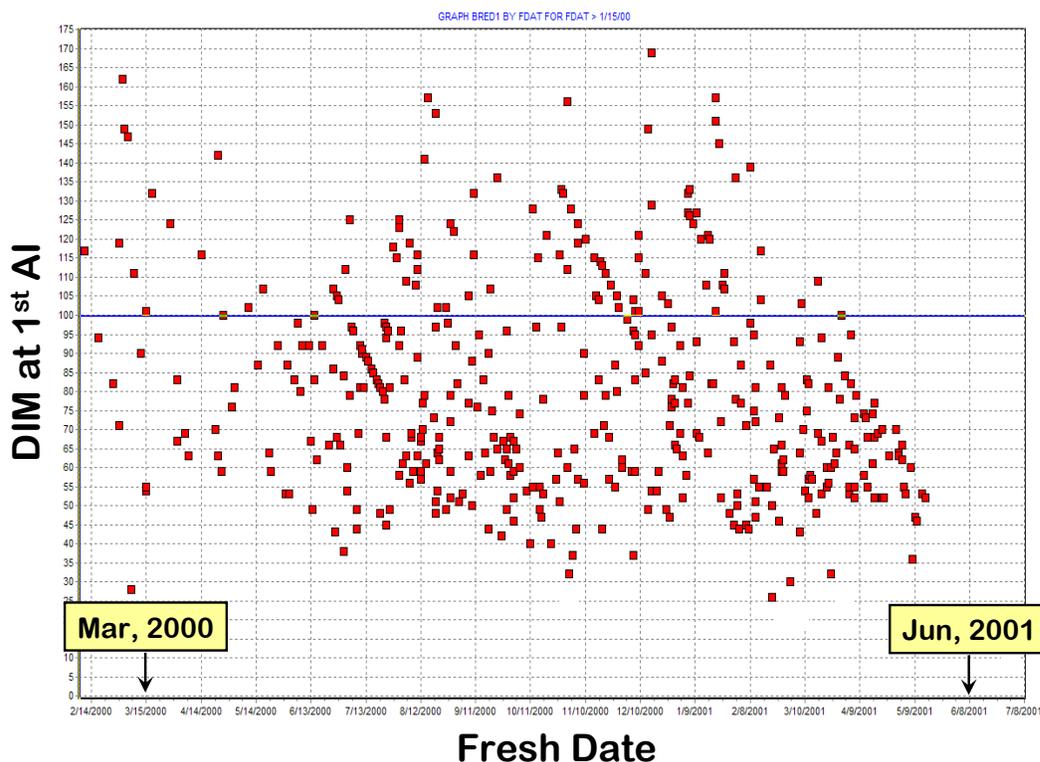


Figure 1. Days in milk at first breeding (y-axis) by date of freshening (x-axis) for cows managed using primarily visual detection of estrus for first postpartum AI service. In this herd, nearly one-third of the cows were serviced for the first time after 100 DIM.

visual estrus detection for AI because of poor estrus detection by dairy personnel and poor estrus expression by lactating dairy cows. Recent reports have estimated that 20-30 % of lactating cows were not cycling by 60 DIM (Pursley et al., 2001; Gümen et al., 2003).

Implementation of Ovsynch Using the *Back-Door* Approach

Figure 2 illustrates a 1,600-cow herd managed using a combination of visual detection of estrus and Ovsynch and TAI for first postpartum AI service. Similar to Figure 1, DIM at first breeding is plotted on the vertical axis (y-axis) and date of freshening (i.e., time) is plotted on the

horizontal axis (x-axis). In this herd, cows failing to be detected in estrus during the first 25 days after the VWP (d 45 to 70) initiate the first GnRH injection of Ovsynch beginning around 70 DIM and receive a TAI 10 d later around 80 DIM. This system is sometimes referred to as the *back-door* Ovsynch approach because Ovsynch is used as a *clean-up* system for cows failing to be detected in estrus. It is not uncommon for Ovsynch to result in a lower CRI than AI to a detected estrus when analyzing and comparing CRI in a herd using the *back-door* Ovsynch approach. This is likely because cows fail to be detected in estrus for reasons due to sickness or injury, or because these cows are anovular. Thus, the expectation should be for a lower CRI to

Distribution of DIM at 1st AI Service: Farm 2

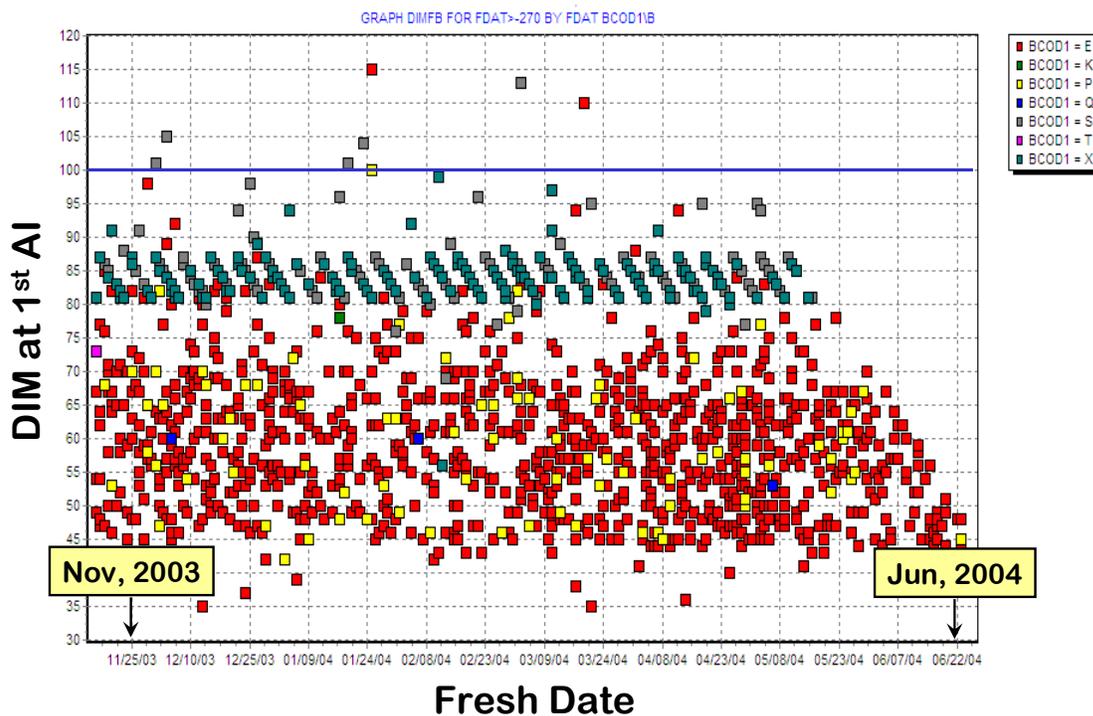


Figure 2. Days in milk at first breeding (y-axis) by date of freshening (x-axis) for cows managed using a combination of visual detection of estrus and Ovsynch and TAI for first postpartum AI service. In this herd, cows failing to be detected in estrus during the first 25 days after the VWP initiated Ovsynch beginning around 70 DIM.

Ovsynch because a subset of cows with poor fertility is exposed to Ovsynch; whereas normally cycling cows are inseminated to a detected estrus.

Programming Cows for First Postpartum AI Using Presynch/Ovsynch

The first results with Ovsynch (Pursley et al., 1995) indicated that all non-pregnant cows could be enrolled into the protocol regardless of their stage during the estrous cycle. Subsequent results from Vasconcelos et al. (1999) using lactating dairy cows, and those of Moreira et al. (2000) using dairy heifers, showed that initiation of Ovsynch between days 5 to 12 of the estrous cycle may result in improved

CRI over the original Ovsynch protocol. Hormonal presynchronization of cows to group randomly cycling cows to initiate Ovsynch between days 5 to 12 of the estrous cycle can be accomplished using two injections of PGF_{2α} administered 14 d apart before initiation of the first GnRH injection of Ovsynch. A presynchronization strategy in which two injections of PGF_{2α} administered 14 d apart preceded initiation of Ovsynch by 12 to 14 d has shown to improve CRI in lactating dairy cows compared to Ovsynch alone (Presynch; Moreira et al., 2001; Navanukraw et al., 2004). For cycling cows, CRI increased from 29 % for Ovsynch to 43 % for Presynch/Ovsynch cows; however, no statistical treatment difference was detected

when all cows (cycling and anovular) were included in the analysis. Thus, use of Presynch for programming lactating dairy cows to receive their first postpartum TAI can improve first service CRI in a dairy herd.

Implementation of a Presynch/Ovsynch Protocol

Use of a controlled breeding program such as Presynch/Ovsynch for initiating first AI service exposes all cows in the herd to the risk of becoming pregnant at or very near the end of the VWP. Figure 3, illustrates a 1,100-cow herd managed using

a Presynch/Ovsynch schedule. Similar to Figures 1 and 2, DIM at first breeding is plotted on the vertical axis (y-axis) and date of freshening (i.e., time) is plotted on the horizontal axis (x-axis). In this herd, nearly all cows receive their first postpartum AI service between 65 and 73 DIM. In this scenario, the end of the VWP is roughly equal to the average day at first service for nearly all cows in the herd. Of course, not all cows will conceive to first service; CRI in lactating dairy cows is poor, and hormonal breeding programs increase PRI by increasing SRI, not fertility.

Distribution of DIM at 1st AI Service: Farm 3

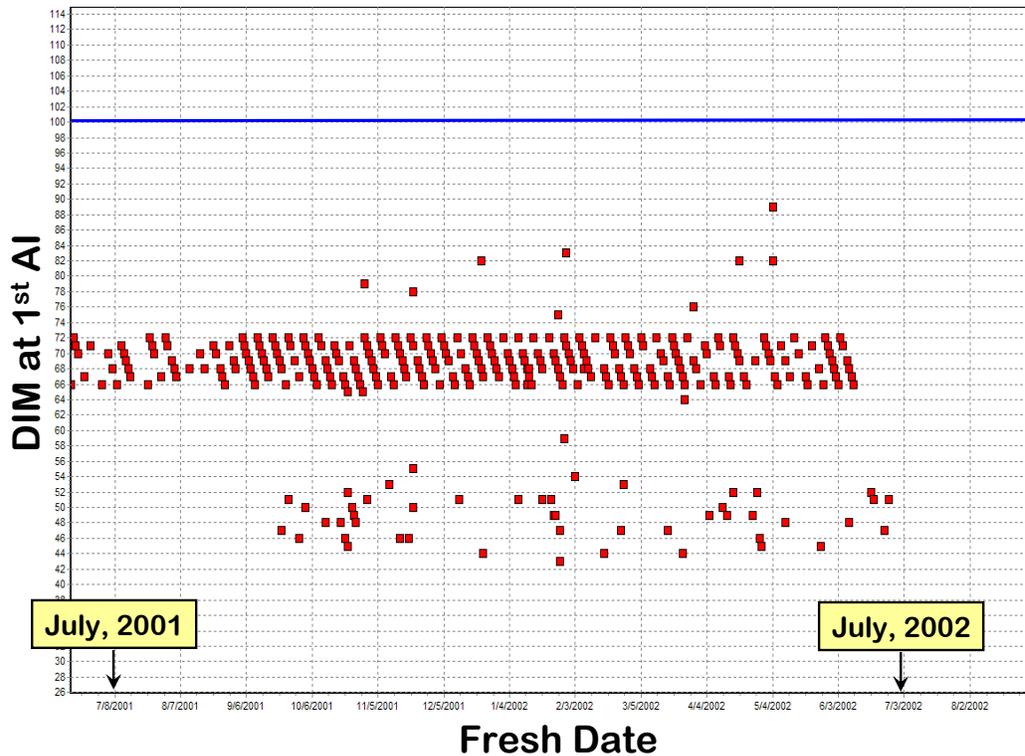


Figure 3. Days in milk at first breeding (y-axis) by date of freshening (x-axis) for cows managed using Presynch/Ovsynch and TAI for first postpartum AI service. In this herd, 98 % of cows received a TAI for first service and less than 5 % of cows received AI after a detected estrus.

Programming First and Second AI Service: Presynch and Resynch

Aggressive reproductive management comprises three strategies that can be implemented early during the breeding period of lactating dairy cows: 1) submit all cows for first postpartum AI service at the end of the VWP, 2) identify non-pregnant cows after AI, and 3) return cows failing to conceive to first AI service to second AI service. Timely rebreeding of lactating dairy cows that fail to conceive to first AI service is essential for improving reproductive efficiency and profitability in a dairy herd. Because AI CRI of high producing lactating dairy cows are reported to be 40 % or less (Pursley et al., 1997; Fricke et al., 1998), 60 % or more of lactating cows will fail to conceive to a given AI service. Now that it is relatively easy to program cows for first postpartum AI service, many producers are asking how best to identify non-pregnant cows and program them for second and subsequent AI services.

Resynch Study 1

We conducted a field trial to test such a system on a herd comprised of 1,100 lactating Holstein cows in north-central Wisconsin (Fricke et al., 2003). Our objective was to compare CRI to first TAI service after a modified Presynch/Ovsynch protocol with CR after Resynch of ovulation using Ovsynch at three intervals after TAI. Lactating dairy cows (n =711) were enrolled into this study on a weekly basis beginning on May 10, 2001 and ending on May 30, 2002. All cows received a modified Presynch/Ovsynch protocol to receive first postpartum TAI as follows: 25 mg PGF_{2α} (d 32 ± 3; d 46 ± 3); 50 µg GnRH (d 60 ± 3); 25 mg PGF_{2α} (d 67 ± 3) and 50 µg GnRH (d 69 ± 3) postpartum. All cows received TAI immediately after the second GnRH

injection of the Presynch/Ovsynch protocol (d 0) as per a Cosynch TAI schedule. At first TAI, cows were randomly assigned to each of three treatments for Resynch of ovulation using Ovsynch [50 µg GnRH (d -9); 25 mg PGF_{2α} (d -2) and 50 µg GnRH + TAI (d -0)] to induce a second TAI for cows failing to conceive to first TAI service. All cows (n=235) in the first treatment (D 19) received a GnRH injection on d 19 post TAI and continued the Ovsynch protocol if diagnosed non-pregnant using transrectal ultrasound on d 26 post TAI. Cows (n=240) in the second (D 26) and cows (n=236) in the third (D 33) treatments initiated the Ovsynch protocol if diagnosed nonpregnant using transrectal ultrasound on d 26 or d 33 after TAI, respectively.

Results from this study argue against the D19 treatment interval as a viable Resynch strategy based on a poor CRI after the Resynch TAI. A veterinarian who can accurately determine pregnancy status via rectal palpation 33 d post TAI could incorporate the D33 Resynch strategy without reliance on transrectal ultrasound for early pregnancy diagnosis. Another option is that all cows could be administered GnRH at 33 d after TAI. Cows would then receive PGF_{2α} at a nonpregnancy diagnosis conducted one week later. In fact, many options for setting the day of nonpregnancy diagnosis are workable in an on-farm management system such that nonpregnancy diagnosis can occur any day between the first GnRH injection and the PGF_{2α} injection of Resynch to accommodate the schedules of the farm as well as the veterinarian.

One difficulty in interpreting fertility to the D26 and D33 Resynch treatments in this first study was that pregnancy diagnosis was conducted at 26 d after TAI for the D26 Resynch and at 33 d for the D33 Resynch; thus confounding a direct comparison of

CRI between these treatments. We therefore conducted a follow-up study.

Resynch Study 2

The objective of this study (Sterry et al., 2006) was to evaluate CRI for cows in which the first GnRH injection of Resynch was initiated either 26 or 33 d after an initial TAI with nonpregnancy assessed 33 d after initial TAI for both treatments. A second objective was to determine the rate of PL at specific points after TAI for both the initial and Resynch TAI. Based on the results of Fricke et al. (2003), our hypothesis was that initiation of Resynch 33 d after TAI would yield a higher CRI compared to initiation of Resynch 26 d after TAI.

Lactating Holstein cows (n=767) at various DIM and prior AI services were randomly assigned at TAI to receive the first GnRH of Ovsynch 26 d (D26) or 33 d (D33) after an initial TAI to Resynch cows failing to conceive to the initial TAI (100 µg GnRH, d 0, 25 mg PGF_{2α}, d 7, 100 µg GnRH+TAI, d 9). All D26 cows received GnRH 26 d after TAI and continued Ovsynch only if diagnosed nonpregnant using ultrasonography 33 d after TAI; whereas all D33 cows initiated Ovsynch only if diagnosed nonpregnant 33 d after TAI. Cows receiving initial TAI as their first postpartum TAI after Presynch/Ovsynch had a greater CRI than cows receiving Resynch for second and greater postpartum TAI (54 vs. 38 %). Pregnancy loss after initial TAI was 3.7 % from 33 to 40 d, and 3.3 % from 40 to 61 d. Cows failing to conceive to initial TAI were classified as either having or lacking a CL > 10 mm at the nonpregnancy diagnosis. There was a treatment by parity interaction for CRI after Resynch for cows with a CL at nonpregnancy diagnosis. Primiparous cows

had a greater CRI when Resynch was initiated 33 d vs. 26 d after initial TAI; whereas CRI for multiparous cows did not differ between treatments and was similar to primiparous cows in which Resynch was initiated 26 d after initial TAI. Pregnancy loss for Resynch cows with a CL at nonpregnancy diagnosis did not differ between treatments and was 6.7 % from 33 to 40 d and 4.1 % from 40 to 61 d after Resynch TAI.

Based on these results from Sterry et al. (2006), submission of cows for first postpartum TAI after Presynch/Ovsynch yielded a greater CRI than submission of cows for second and greater postpartum TAI after Resynch, and delaying initiation of Resynch until 33 d after initial TAI increased CRI for primiparous, but not multiparous, cows. A graphic illustration of the timing of first postpartum TAI and subsequent Resynch TAI for a farm in Wisconsin that almost exclusively relies on a Synch and Resynch system using the 33 d interval between initial TAI and initiation of Resynch to inseminate cows is shown in Figure 4. We currently are conducting a third study on a different dairy in Wisconsin in which cows are resynchronized 25 or 32 d after TAI. It will be interesting to see whether this treatment by parity interaction is evident in that data set.

Effect of Increasing Progesterone Post-TAI

Several studies have reported that cows diagnosed pregnant to an insemination retrospectively had greater circulating progesterone concentrations early after AI compared with cows failing to conceive to AI. A higher concentration of progesterone as early as 4 to 5 d (Gümen et al., 2003) or 6 d after AI to a spontaneous estrus has been

Distribution of DIM at latest AI Service: Farm 3

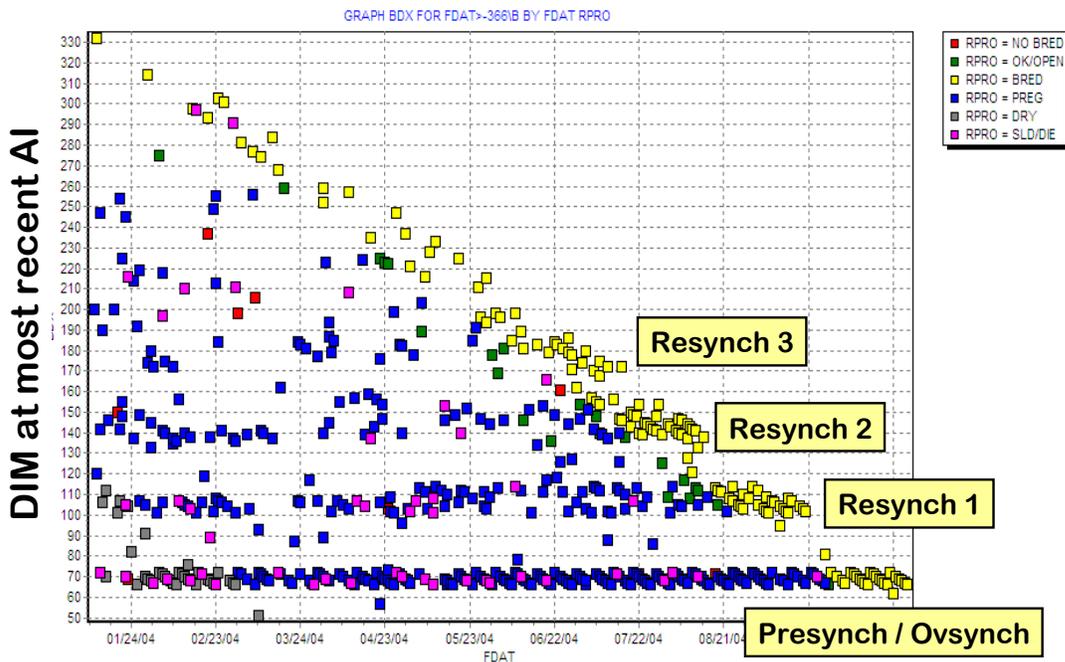


Figure 4. Days in milk at most recent breeding (y-axis) by date of freshening (x-axis) for cows managed using a systematic Synch and Resynch approach. In this herd, 98 % of cows receive TAI for first service and less than 5 % of cows received AI after a detected estrus.

reported for pregnant cows (Henricks et al., 1971; Ahmad et al., 1996). Henricks and Dickey (1970) and Lukaszewska and Hansel (1980) reported that pregnant cows had a greater serum progesterone concentration than nonpregnant cows as early as d 10 of pregnancy. Furthermore, a delay in the postovulatory rise of progesterone was observed in nonpregnant versus pregnant cows (Mann and Lamming, 2001).

As discussed by Gümen et al. (2003), some studies have suggested that the increase in circulating progesterone may be critical for optimal embryo development (Garrett et al., 1988; Kleemann et al., 1994; Mann and Lamming, 2001). Alternatively, the embryo may secrete luteotropic

substances that could increase circulating progesterone in pregnant cows (Thibodeaux et al., 1994). Although the observation of greater progesterone in pregnant cows early after AI is associative rather than causative, some have speculated that increasing progesterone early after AI either exogenously or endogenously may improve CRI or reduce PL in lactating dairy cows. We conducted the following study to test this hypothesis (Sterry et al., 2005).

In two experiments, lactating Holstein cows received their first postpartum (PP) TAI after a Presynch/Ovsynch protocol using 25 mg $\text{PGF}_{2\alpha}$ and 100 μg GnRH as follows: $\text{PGF}_{2\alpha}$ (32 ± 3 and 46 ± 3 d PP); GnRH (60 ± 3 d

PP); PGF_{2α} (67 ± 3 d PP); GnRH+TAI (69 ± 3 d PP). Cows without a CL >10 mm at the first injection of GnRH were classified as anovular and were treated with a CIDR (Pfizer, Inc., New York, NY). Cows (n=674) in Experiment 1 were randomized to each of three treatments to receive: 1) no treatment (C; n=226), 2) 100 µg GnRH 5 d after TAI (G5; n=228), or 3) CIDR from 5 to 12 d after TAI (CIDR; n=220). For pregnant cows, number of CL 33 d after TAI was greater (P < 0.01) for G5 (1.8 ± 0.1) than for C (1.3 ± 0.1) or CIDR (1.3 ± 0.1) cows. Treatment did not affect CR 33 d after TAI (50, 55, and 47 %, respectively) or PL from 33 to 61 d after TAI (8 %, overall). Overall, 23 % of cows were anovular, and CR at 33 d was greater (P < 0.01) for cycling (54 %) than for anovular (40 %) cows; whereas PL from 33 to 61 d was greater (P < 0.01) for anovular (16 %) than for cycling (8 %) cows. Cows in Experiment 2 (n=485) were randomized to each of three treatments to receive: 1) C (n=163), 2) G5 (n=158), or 3) 100 µg GnRH 7 d after TAI (G7; n=164). For pregnant cows, number of CL 33 d after TAI was greater (P < 0.01) for G5 (1.6 ± 0.1) and G7 (1.7 ± 0.1) than for C (1.2 ± 0.1) cows. Treatment did not affect CR 33 d after TAI (51, 49, and 53 %, respectively). Overall, 26 % of cows were anovular, and CR at 33 d was greater (P < 0.05) for cycling (55 %) than for anovular (43 %) cows; whereas PL from 33 to 61 d was greater (P < 0.01) for anovular (13 %) than for cycling (8 %) cows. When C (n=389) and G5 (n=386) cows from Experiments 1 and 2 were combined and analyzed, treatment did not affect CRI 33 d after TAI (50 vs. 53 %, respectively) or PL from 33 to 61 d after TAI.

Based on these results, we concluded that although administration of GnRH or CIDR inserts early after first PP TAI did not affect CRI or PL in lactating Holstein cows,

cyclicity status before TAI affected fertility with cycling cows yielding higher CRI and lower PL than anovular cows.

Protocol Compliance Is Key

The physiology that underlies the hormonal protocols that allow for TAI such as Ovsynch and Presynch has been researched extensively and continues to be a topic of active investigation among dairy scientists studying reproductive biology. Physiologic scenarios leading to reduced performance of these protocols or the mechanisms by which these protocols may improve reproduction have been reported and reviewed (Cordoba and Fricke, 2002; Navanukraw et al., 2004). Both scientific research and anecdotal evidence supports the idea that Ovsynch and Presynch work well for high producing dairy cows in North America managed under confinement systems. Many factors affect reproductive performance, and many consultants have observed a wide range of performance among farms that have adopted the exact same protocol. Reduced performance of these protocols is rarely due to physiologic responses of individual cows to the hormonal protocol, but almost always can be attributed to compliance issues at the farm level.

To achieve success with these hormonal protocols, each farm has to develop a system to administer the correct injections to the correct cows on the correct days, then subsequently AI the correct cows. A standard Presynch/Ovsynch protocol for submitting cows for first AI service requires that each individual cow receive 5 consecutive injections at the appropriate injection intervals. Failure to administer any one of these 5 injections dramatically or completely reduces the CRI to first TAI and will ultimately result in a delay in

establishing pregnancy. For a farm that achieves an injection protocol accuracy of 95 % on any given injection day (e.g., 95 % of the cows that should get an injection actually get the correct one), on average nearly one in four cows will not successfully complete the 5 injections of the Presynch/Ovsynch protocol (e.g., $0.95 \times 0.95 \times 0.95 \times 0.95 = 0.77$). Thus, nothing less than 100 % protocol compliance should be considered acceptable. Therefore, farms that cannot achieve near 100 % protocol compliance should consider focusing on other methods to improve SRI including heat detection and heat detection aids.

References

- Ahmad, N., S. W. Beam, W. R. Butler, D. R. Deaver, R. T. Duby, D. R. Elder, J. E. Fortune, L. C. Griel, L. S. Jones, R. A. Milvae, J. L. Pate, I. Revah, D. T. Schreiber, D. H. Townson, P. C. W. Tsang, and E. K. Inskeep. 1996. Cooperative Regional Research Project. NE-161. Relationship of fertility to patterns of ovarian follicular development and associated hormonal profiles in dairy cows and heifers. *J. Anim. Sci.* 74:1943–1952.
- Cordoba, M. C., and P. M. Fricke. 2002. Initiation of the breeding season in a grazing-based dairy by synchronization of ovulation. *J. Dairy Sci.* 85:1752–1763.
- Fricke, P. M., J. N. Guenther, and M. C. Wiltbank. 1998. Efficacy of decreasing the dose of GnRH used in a protocol for synchronization of ovulation and timed AI in lactating dairy cows. *Theriogenology* 50:1275–1284.
- Fricke, P. M., D. Z. Caraviello, K. A. Weigel, and M. L. Welle. 2003. Fertility of dairy cows after resynchronization of ovulation at three intervals after first timed insemination. *J. Dairy Sci.* 86:3941–3950.
- Garrett, J. E., R. D. Geisert, M. T. Zavy, and G. L. Morgan. 1988. Evidence for maternal regulation of early conceptus growth and development in beef cattle. *J. Reprod. Fertil.* 84:437–446.
- Gümen, A., J. N. Guenther, and M. C. Wiltbank. 2003. Follicular size and response to Ovsynch versus detection of estrus in anovular and ovular lactating dairy cows. *J. Dairy Sci.* 86:3184–3194.
- Henricks, D. M., and J. F. Dickey. 1970. Serum luteinizing hormone and plasma progesterone levels during the estrous cycle and early pregnancy in cows. *Biol. Reprod.* 2:346–351.
- Henricks, D. M., D. R. Lamond, J. R. Hill, and J. F. Dickey. 1971. Plasma progesterone concentrations before mating and in early pregnancy in the beef heifer. *J. Anim. Sci.* 33:450–454.
- Kleemann, D. O., S. K. Walker, and R. F. Seamark. 1994. Enhanced fetal growth in sheep administered progesterone during the first three days of pregnancy. *J. Reprod. Fertil.* 102:411–417.
- Lukaszewska, J., and W. Hansel. 1980. Corpus luteum maintenance during early pregnancy in the cow. *J. Reprod. Fertil.* 59:485–493.
- Mann, G. E., and G. E. Lamming. 2001. Relationship between maternal endocrine environment, early embryo development and inhibition of the luteolytic mechanism in cows. *Reproduction* 121:175–180.
- Moreira, F., R. L. de la Sota, T. Diaz, and W. W. Thatcher. 2000. Effect of day of the estrous cycle at the initiation of a timed artificial insemination protocol on reproductive responses in dairy heifers. *J. Anim. Sci.* 78:1568–1576.
- Moreira, F., C. Orlandi, C. A. Risco, R. Mattos, F. Lopes, and W. W. Thatcher. 2001. Effects of presynchronization and bovine somatotropin on pregnancy rates to a timed artificial insemination protocol in lactating dairy cows. *J. Dairy Sci.* 84:1646–1659.
- Navanukraw, C., L. P. Reynolds, J. D. Kirsch, A. T. Grazul-Bilska, D. A. Redmer, and P. M. Fricke. 2004. A modified presynchronization protocol improves fertility to timed artificial insemination in lactating dairy cows. *J. Dairy Sci.* 87:1551–1557.
- Pursley, J. R., M. O. Mee, and M. C. Wiltbank. 1995. Synchronization of ovulation in dairy cows using PGF_{2α} and GnRH. *Theriogenology* 44:915–923.
- Pursley, J. R., M. R. Kosorok, and M. C. Wiltbank. 1997. Reproductive management of lactating dairy cows using synchronization of ovulation. *J. Dairy Sci.* 80:301–306.

Pursley, J. R., P. M. Fricke, H. A. Garverick, D. J. Kesler, J. S. Ottobre, J. S. Stevenson, and M. C. Wiltbank. 2001. NC-113 Regional Research Project. Improved fertility in anovulatory lactating dairy cows treated with exogenous progesterone during Ovsynch. *J. Dairy Sci.* (Midwest Branch ADSA Meetings, Des Moines, IA, Abstract 251 p. 63).

Sterry, R. A., M. L. Welle, and P. M. Fricke. 2006. Effect of interval from timed AI to initiation of resynchronization of ovulation using Ovsynch on fertility of lactating dairy cows. *J. Dairy Sci.* (In press).

Sterry, R. A., M. L. Welle, and P. M. Fricke. 2005. Effect of GnRH or CIDR inserts administered early

after first timed insemination on fertility of lactating dairy cows. *J. Dairy Sci.* 88(Suppl. 1):87 (Abstr.).

Thibodeaux, J. K., J. R. Broussard, R. A. Godke, and W. Hansel. 1994. Stimulation of progesterone production in bovine luteal cells by co-incubation with bovine blastocyst-stage embryos or trophoblastic vesicles. *J. Reprod. Fertil.* 101:657-662.

Vasconcelos, J. L. M., R. W. Silcox, G. J. Rosa, J. R. Pursley, and M. C. Wiltbank. 1999. Synchronization rate, size of the ovulatory follicle, and pregnancy rate after synchronization of ovulation beginning on different days of the estrous cycle in lactating dairy cows. *Theriogenology* 52:1067-1078.