Practical Manipulation of the Estrous Cycle in Dairy Animals

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Introduction

Considerable advancements in reproductive biology and technology have occurred over the past 15 years that are useful tools to dairy producers to improve reproductive management of heifers and lactating dairy cows. These are even more important when we deal with increasing herd size and cope with seasonal periods of reduced fertility, such as in the south, due to heat stress. Utilization of these tools needs to be founded on a thorough understanding of the reproductive events that they control, and implemented in a manner that is compatible with: the cow, the management system, goals of the farm, and the veterinarian or staff responsible for the health care of the cattle. It is clear to all who have managed dairy cows that use of drugs that regulate reproductive events are no substitute for good management. Indeed, they will only work efficiently if management is good.

Our current knowledge to successfully manipulate the estrous cycle, control the time of ovulation, and to enhance embryo survival in dairy cattle has provided the dairy industry with new and novel strategies of reproductive management. Optimization of reproductive management in lactating dairy cows is a challenge in that reproductive performance has declined with increasing milk production of the herd.[4] Our comprehension of the various factors controlling ovarian follicle development, intensity of estrous behavior, corpus luteum development and regression, and time of ovulation has led to several tested strategies to improve reproductive management in dairy cattle. **It is important to recognize that in the United States only two classes of drugs are approved currently for use in lactating dairy cows. They include Gonadotrophin Releasing Hormone and its analogues (GnRH) and Prostaglandin (PG) $F_{2\alpha}$ and its analogues ($PGF_{2\alpha}$).** Other compounds like various progestins and estrogens that have been utilized in dairy heifers, beef heifers and beef cows have not been approved for use in lactating dairy cows. An additional exciting aspect of applying current reproductive technology to control and improve reproductive management is that new and basic strategies can be investigated and applied to improve fertility by increasing conception rates or embryo survival.

Several studies have documented that conception rates are increased after 60 days postpartum, and this is associated undoubtedly with improved uterine health and body condition, and increasing energy balance. The opportunity for producers to take advantage of this relationship has been hampered by inefficient detection of estrus leading to an inability to control precisely time of first service on a herd basis. Herd pregnancy rates are the product of estrus detection and conception rates. It is not practical to recommend producers to delay first service or to set the voluntary waiting period until 70 days if heat detection rates are only 50%. At this level of reproductive management, a producer would need to begin heat detection and inseminations at approximately 50 days postpartum to have a mean interval of first service of 70 days. Furthermore, the range of day to first service would be between 50 to 90 days postpartum. In contrast, if time of ovulation and first service can be controlled precisely, then a great increase in efficiency of reproductive management can be achieved with all inseminations made precisely at day 70 postpartum. This permits a programmed delay in the necessity to heat detect and inseminate cows until after 70 days postpartum, and first service is made when factors associated with optimal postpartum fertility are in place. Such strategies are reasonable for producers to implement and are cost effective.

The objective of this presentation is to integrate the various reproductive strategies that are currently available for application in dairy animals.

Use of Prostaglandin (PG) $F_{2\alpha}$

It is a major challenge in large herds to maintain an efficient level of herd fertility. Currently, the average days open for Florida dairies enrolled in the DHI program is 142 days or the minimum projected calving interval for cows that conceived is 14.0 months. From a realistic management approach, the most efficient manner to reduce days open is to reduce the number of missed heats and increase the rate of submission of animals for insemination. Utilizing an average conception rate of 40%, the average days open for heat detection rates of 50%, 60%, 70%, 80% and 90% are 154, 136, 124, 115, and 107 days, respectively. Thus, it is clear that strategies to decrease the days before animals begin to cycle, and increase the rate that animals are presented for insemination will be effective in reducing days open. Systems of effective estrous synchronization in which groups of animals are programmed to express heat should effectively reduce days open. Currently strategies to improve conception rates will not be as effective or as dramatic to increase reproductive efficiency as systems that effectively synchronize heats and increase heat detection rates. Groups of animals that are in heat increase the probability of accurate estrus detection because of more active animal to animal interactions. Any system to increase estrus detection rates (chalk, heat mount detectors, pedometers etc.) will be useful.

Utilization of $PGF_{2\alpha}$ for estrous synchronization is an excellent reproductive management tool. Prostaglandin $_{2\alpha}$ is an extremely potent fatty acid-like substance produced in many tissues of the body and most specifically by the uterus. Indeed, $PGF_{2\alpha}$ is the natural substance produced by the uterus of the cow to cause normal regression of the corpus luteum. Thus, injection of $PGF_{2\alpha}$ is a means to selectively induce regression of the corpus luteum in a manner that mimics the normal process. Numerous fertility trials indicate a normal fertility to inseminations made at the induced heat and that conception rates will be at least comparable to what is characteristic of the herd. Cattle cannot be injected with $PGF_{2\alpha}$ at all stages of the estrous cycle because the newly-induced corpus luteum will not respond or undergo induced regression. Cows injected between days 1 to 5 of the estrous cycle are essentially non-responsive to induced CL regression by $PGF_{2\alpha}$. Cows injected between days 7 to 16 are responsive to injections of $PGF_{2\alpha}$. However, there is a clear pattern of response in which animals injected on days 7, 15 and 16 are more precisely synchronized with the incidence of induced heats being higher on day 3 after injection of $PGF_{2\alpha}$. A greater proportion of cows injected on days 8 to 14 have heats on days 4 to 7 after $PGF_{2\alpha}$ injection.[24] We now know that this differential pattern is related to the occurrence of follicular waves during the estrous cycle.[22,41] Ovarian follicles are in optimal health on day 7 and begin to enter a plateau phase of growth and undergo atresia between ~ days 9 to 12 of the estrous cycle. At about day 12, a new follicle wave begins to occur. By day 15 this second wave follicle is large and healthy so that when $PGF_{2\alpha}$ is injected, cows come into heat at a high frequency by day 3 after injection of $PGF_{2\alpha}$. Between days 8 to 15, a higher proportion of first wave follicles do not ovulate and the longer intervals to occurrence of heat is associated with a period of waiting for the second wave follicle to develop and induce a heat. Thus, the pattern of heats after $PGF_{2\alpha}$ injection is associated with stage of ovarian follicular development. $PGF_{2\alpha}$ was first approved for heifers or non-lactating cows. The recommendation was to inject $PGF_{2\alpha}$ twice 11 days apart. Such a treatment program increases the number of animals in a $PGF_{2\alpha}$ responsive phase at the second injection (e.g., all have a CL sensitive to $PGF_{2\alpha}$), and these heifers will tend to be in the correct phases of either the first or second follicular wave to improve the precision of estrous synchrony. With heifers, injecting $PGF_{2\alpha}$ twice 11 days apart gives an estrous response of 85% under field conditions.[50] In lactating dairy cows, the metabolic and hormonal changes associated with lactation alter ovarian follicular development. This is supported by a reduction in plasma estradiol and altered patterns of follicular growth compared to non-lactating dairy cows[7] such that lactating cows come into heat later than heifers and non-lactating cows. Thus, an 11-day interval between $PGF_{2\alpha}$ injections will make a higher proportion of cows at an earlier stage of the estrous cycle at the time of second injection. In this situation, $PGF_{2\alpha}$ may fail to regress CL that are in a non-responsive stage (days 1 to 5 of the cycle). In a field study that compared an 11 versus a 14-day injection for $PGF_{2\alpha}$ in primiparous cows,[14] the 14-day interval increased percent of pregnant cows within 30 days of first insemination (84.2 versus 61.9%) and reduced days open for pregnant cows (118 versus 141 days). Because of these observations, a 14-day injection interval is recommended for lactating dairy cows.[11] Such an interval lends itself to weekly visits for scheduling reproductive management tasks. A 7-day interval between $PGF_{2\alpha}$ would not insure that all cows would be in a responsive stage of the estrous cycle at the second injection.

With this background, several strategies have been developed to use repeated injections of $PGF_{2\alpha}$ as a tool to induce estrus at the time of the voluntary waiting period. Usually a set-up injection of $PGF_{2\alpha}$ is administered to increase the probability that cows contain a mid-cycle CL when their next injection of $PGF_{2\alpha}$ is given close to the designated voluntary waiting period for first service. This approach will synchronize estrus, increase the pool of active cows that will improve heat detection rates, reduce labor for heat detection, and allow for grouping of cows that will reduce frequency of veterinary visits for pregnancy diagnosis.

Weekly Injections of $PGF_{2\alpha}$

Lactating dairy cows that were open received weekly injections of $PGF_{2\alpha}$ beginning at 50 days postpartum and were inseminated at detected estrus.[20] This strategy was compared to open cows that received an injection of $PGF_{2\alpha}$ if the veterinarian identified the presence of a CL at palpation and cows were inseminated at detected estrus. Cows not exhibiting estrus were examined at the next veterinary visit (every 2 weeks for three farms and weekly for one farm) and received $PGF_{2\alpha}$ if a CL was present at palpation. Cows receiving weekly doses of $PGF_{2\alpha}$ had a 30% higher pregnancy rate, a 13-day reduction in median days open (97 versus 110 days), and a smaller interval to first insemination (72.7 versus 78.3 days) compared to the rectal palpation group. Overall agreement between diagnosis of a CL and progesterone is approximately 77% which indicates that rectal palpation is inadequate for identifying cows for $PGF_{2\alpha}$ injection.[19,25] This contributed to the longer interval until first insemination and a lower cumulative pregnancy rate at various stages postpartum for the rectal palpation management group. Because cows must be in the luteal phase of the estrous cycle to respond to $PGF_{2\alpha}$ injections, repeated weekly injections of $PGF_{2\alpha}$ in the same animal will not put the cow in the responsive luteal phase of the cycle as opposed to repeated injections given 14 days apart. As will be discussed later, cows with a high luteal phase progesterone concentration just prior to $PGF_{2\alpha}$ injection for induction of estrus will be more fertile. Thus, the process of injecting cows on a weekly basis does not favor a management scenario that will maximize ability to detect heats and conception rate. Nevertheless, a comparison of these two management scenarios indicated that a weekly injection of $PGF_{2\alpha}$ had a reproductive advantage, and the increased cost per cow of $3.73 due to extra drug cost is more than offset by the economic return of improved pregnancy rate and less days open (13 days x $2.00 per day = $26 per cow).

A single injection of $PGF_{2\alpha}$ at 6 days after the beginning of the breeding period reduced the interval from the beginning of the breeding period to first service from 26 days to 18 days.[44] This reduction in interval to first service occurred even in the face of delaying potential insemination by 6 days in the $PGF_{2\alpha}$ treated group. As a consequence of $PGF_{2\alpha}$ treatment, rates of insemination during the 5 days after $PGF_{2\alpha}$ injection were increased from 21% to 54%. Although conception rates did not differ to these first services, the pregnancy rates were enhanced from 8% for the control group to 23% in the $PGF_{2\alpha}$ treatment group. By synchronizing estrus with $PGF_{2\alpha}$, cows are getting pregnant sooner and that is a reproductive management advantage. Routine manipulation of the estrus cycle with $PGF_{2\alpha}$ treatments has led to the concept of targeted breeding.

Targeted Breeding with $PGF_{2\alpha}$

Ferguson and Galligan[11] implemented a "Prostaglandin Synchronization Program" that is initiated at a time consistent with an established voluntary waiting period designated by the producer as to when cows should be inseminated. For example, with a voluntary waiting period of approximately 55 days, the first injection of $PGF_{2\alpha}$ would be made in all animals > 50 days postpartum. All eligible cows could be injected on a Monday with likely occurrence of heats on Wednesday, Thursday and Friday. Cows detected in heat will be inseminated at detected estrus. At 14 days following the first $PGF_{2\alpha}$ injection, all cows not detected in heat can be injected with $PGF_{2\alpha}$ and inseminated at detected heat. With such a system, over 90% of the cows should be inseminated following two injections of PGF_2 given 14 days apart. Monitoring heat detection rates will also give an indication of how operationally efficient is the local management system. For example, a goal of inseminating 70% of the cows following first injection can be established. If heat detection rates fall below 50%, techniques of heat detection or anestrous status of the cows should be evaluated. At the second $PGF_{2\alpha}$ injection, new cows approaching the voluntary waiting period can receive their first injection of $PGF_{2\alpha}$. Cows are rebred if seen in heat 21 days later. Cows are checked for pregnancy 32-40 days after breeding in a week following a $PGF_{2\alpha}$ injection. If diagnosed open, they re-enter the pool of animals to be treated with $PGF_{2\alpha}$. This system is repeated as a routine management program. Herd inseminators focus on heat detection during designated periods with cows easily targeted because of chalked tail heads. Results from this program are very encouraging as evident by the decrease in the percentage of open cows during lactation compared to previous years when the program was not implemented. Reasonable goals suggested by Ferguson and Galligan[11] are to obtain 80% of cows inseminated by the voluntary waiting period plus 20 days (e.g., 55 + 20 = 75 days postpartum). The ratio of $PGF_{2\alpha}$ injections per total inseminations should be less than 1.55.

Pankowski and coworkers[26] reported on a management system involving the repeated use of $PGF_{2\alpha}$ as a postpartum reproductive management tool. Cows received $PGF_{2\alpha}$ injections at 25 to 32 days postpartum for reproductive therapy with an additional injection of $PGF_{2\alpha}$ for synchronization of estrus at 39 to 46 days. This was followed 14 days later by an additional injection of $PGF_{2\alpha}$ at 53 to 60 days postpartum with initial insemination made following this last injection. Cows not inseminated following the $PGF_{2\alpha}$ injection between 53 to 60 days were retreated with $PGF_{2\alpha}$ 14 days later. This program was compared to cows on a postpartum program of rectal palpation based on veterinary intervention or to a program in which cows only received an injection of $PGF_{2\alpha}$ at 25 to 32 days for reproductive therapy. All three groups received an injection of $PGF_{2\alpha}$ at 53 to 60 days to insure an equivalent initial breeding for each treatment. The reproductive management program with repeated injections of $PGF_{2\alpha}$ had a 11% higher rate of synchronized first inseminations that contributed to a 10% higher pregnancy rate than cows of the rectal palpation and reproductive therapy groups. Median days to first insemination was 63 days versus 71 days and median days open was 107 days versus 113 days for the repeated $PGF_{2\alpha}$ program compared to the other two groups. This reproductive advantage is due to cows receiving three $PGF_{2\alpha}$ injections prior to insemination. The greater number of $PGF_{2\alpha}$ injections resulted in a greater synchronization of estrus and an earlier occurrence to first insemination. This resulted in a reproductive advantage for the repeated $PGF_{2\alpha}$ group that reduced net cost per cow by $15.61 compared to the rectal palpation group. This system of repeated $PGF_{2\alpha}$ injections is the basis for targeted breeding.

Dr. Roy Fogwell at Michigan State University[12] has defined and described the concept of a Targeted Breeding Program (http;//www.canr.msu.edu/dept/ans/mdr119.html) and is described as follows. Targeted Breeding is a program that employs synchronization of estrus (heat) at scheduled times. High detection of estrus within groups of cows will lead to a timely artificial insemination (AI) and ultimately to a high pregnancy rate early in the breeding period. The concept is to control estrus artificially so that for a group of cows, estrus and AI are scheduled for specific days early in the breeding period. These days are the target. For Targeted Breeding, timing of estrus is controlled by injection of $PGF_{2\alpha}$. The sequence of events for Targeted Breeding is illustrated in Figure 1. Dr. Fogwell points out that it is important to recognize that a minimal goal of Targeted Breeding is that all cows in a breeding group are detected in estrus and inseminated at least once within the first 21 days of the "Breeding Period". If all cows are experiencing estrous cycles by 46 days after

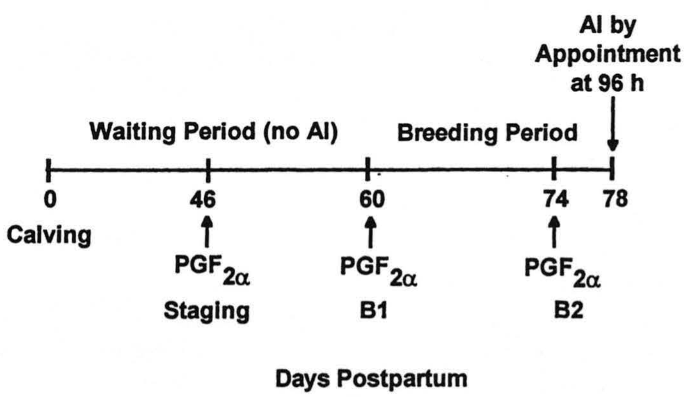


Figure 1. Targeted Breeding Program

calving and if detection of estrus is 100 percent, this goal can be achieved with two injections of $PGF_{2\alpha}$. The first injection of $PGF_{2\alpha}$ is labeled the "Staging Injection" and occurs during the "Waiting Period" at 14 days before the "Breeding Period". The "Staging Injection" of $PGF_{2\alpha}$ is critical to make all cows responsive to $PGF_{2\alpha}$ at onset of the "Breeding Period". Thus, all cows should exhibit estrus and receive AI within 5 days after start of the breeding period. In addition, detection of estrus after the "Staging Injection" of $PGF_{2\alpha}$ can help evaluate skills of estrus detection and status of the cows. With a single injection of $PGF_{2\alpha}$, an average of 75 percent of cows should exhibit estrus within 5 days. If less than 50 percent of injected cows are detected in estrus then a problem exists. The problem could be that some cows have not started estrous cycles since calving (anovulatory), or the problem could be poor detection of estrus by personnel. The important point is to determine whether there is a problem, determine the cause of the problem and take corrective action before the second injection of $PGF_{2\alpha}$.

At onset of the Breeding Period, 14 days after Staging $PGF_{2\alpha}$, cows receive a second injection of $PGF_{2\alpha}$ labeled the first breeding injection ($PGF_{2\alpha}$-B1). For 5 days after this injection, cows are observed for estrus and only those cows detected in estrus are inseminated. Insemination should occur 8 to 12 hours after estrus is first detected. Cows not detected in estrus after PGF2 receive another injection of $PGF_{2\alpha}$ 14 days after $PGF_{2\alpha}$-B1. This injection is labeled the second breeding injection ($PGF_{2\alpha}$-B2). During the 4 days after $PGF_{2\alpha}$-B2, cows should be observed for estrus and inseminated at 8 to 12 hours after detection of estrus. Cows not detected in estrus by 4 days after $PGF_{2\alpha}$-B2 should be inseminated at 96 hours ("AI by Appointment"). Conception rate with insemination by appointment is at least 20 percent lower than when AI occurs after detected estrus. Dr. Fogwell points out that this difference in fertility should be an incentive to maximize detection of estrus so most or all cows get AI by detected estrus and to maximize return on investment in $PGF_{2\alpha}$.

If you implement Targeted Breeding you can expect the following:

1. Cows will experience estrus according to your schedule. You control week and days of the week that you must observe for estrus and AI.
2. Controlled estrus is predictable and multiple cows in estrus simultaneously (synchronized) will increase duration and intensity of estrus. Thus, success of detecting estrus will increase.
3. All cows should be inseminated during the first week of the breeding period.
4. With Targeted Breeding, conception rate will not change, but more cows will be inseminated, so more

cows will conceive during the early breeding period (the target).

For this system to work, you must attend to the details of detecting estrus and AI as with any reproductive management activity. Dr. Fogwell places emphasis on the following points to make the program successful.

1. Cows must be healthy and experiencing estrous cycles before the "Staging Injection" of $PGF_{2\alpha}$.

2. After injection of $PGF_{2\alpha}$, observations for estrus must be accurate and thorough. Observations should be for 30 minutes every 6 to 8 hours for 5 days after $PGF_{2\alpha}$.

3. When estrus is synchronized by $PGF_{2\alpha}$, timing AI after estrus and procedures for AI are the same as with a non-synchronized estrus.

4. Facilities to restrain cows for injections and AI are critical to minimize labor and to maximize safety of cows and people.

5. Identification of cows must be clear and unique so the correct cows are injected with $PGF_{2\alpha}$ or inseminated at the proper time.

6. Records must be complete to monitor the current reproductive status of individual cows. For example, list those cows inseminated after $PGF_{2\alpha}$-B1 and therefore these cows must not receive $PGF_{2\alpha}$-B2.

7. The 14-day structure of Targeted Breeding makes it convenient to schedule the veterinarian as a partner in management. After 6 weeks of Targeted Breeding, staging a new group will coincide with checking problem cows and examination of cows for pregnancy. This synchrony of jobs is a benefit to management of your time.

To realize the greatest value of Targeted Breeding, cows that do not conceive to first AI must be identified as soon as possible. Thus, observation of estrus 18 to 24 days after AI must be as intense as observations after $PGF_{2\alpha}$. Observations for repeat estrus after AI will coincide with observing other groups of cows injected recently with $PGF_{2\alpha}$. Cows detected in estrus approximately 21 days after AI should be re-inseminated. All cows that have been inseminated should be examined for pregnancy 35 to 40 days after AI. Cows judged not pregnant should be in estrus within 2 to 6 days. Non-pregnant cows not observed in estrus by 42 days after AI should repeat Targeted Breeding. These cows should be included in a group of cows scheduled for $PGF_{2\alpha}$-B1 (the first breeding injection). The idea is tocreate an opportunity for AI as soon as possible. In addition, use of $PGF_{2\alpha}$ will maintain control of cows by restricting periods of expected estrus to groups of cows scheduled to be observed. With any reproductive management program, problems are more likely if size of groups is too large for the abilities of people or capacity of facilities for injections, observations, and AI. For very large herds, more than 500 cows, you should consider staging a group every week. **I encourage each of you practitioners to check out the Website[12] on Targeted Breeding for additional details, and the opportunity to communicate with Dr. Fogwell regarding his experiences.**

Progesterone and $PGF_{2\alpha}$

Cows with high progesterone concentrations before injection of $PGF_{2\alpha}$ to synchronize estrus have a higher estrus detection[37] and conception rate.[14] This, coupled with observations that cows that conceive had higher luteal phase concentrations of progesterone in the previous cycle,[15] has several implications. First synchronization of estrus following two injections of $PGF_{2\alpha}$ 14 days apart will increase the probability that cows will have luteal phase progesterone concentrations before the second injection of $PGF_{2\alpha}$. This should provide a higher pregnancy rate than $PGF_{2\alpha}$ injections given 7 or 11 days apart in lactating dairy cows.

Secondly, the potential importance of high progesterone has led to development of synchronization and reproductive management programs that combine the administration of progesterone and $PGF_{2\alpha}$. Although an improved progesterone or progestin for use in lactating dairy cows is not available to producers in the United States, it is important to examine their potential use. Considerable efforts are underway for approval of a progestin to be used in lactating dairy cows, and it is being used in other countries. Furthermore, the Synchromate B system can be used in dairy heifers. Folman and coworkers[13,14,37] in Israel have conducted a series of experiments combining the use of a progesterone-releasing intravaginal device (PRID) with $PGF_{2\alpha}$ for synchronization of estrus in lactating dairy cows. They reported several interesting observations. Cows injected with $PGF_{2\alpha}$ 14 days apart had a longer period of progesterone exposure and a greater conception rate than cows injected with $PGF_{2\alpha}$ 11 days apart.[37] Cows that had a higher progesterone concentration at the second $PGF_{2\alpha}$ were more fertile. These observations led to the concept that combining an exogenous progesterone treatment with $PGF_{2\alpha}$ may increase reproductive performance. Cows given $PGF_{2\alpha}$ 14 days apart and a PRID for 7 days beginning at day 8 after the first injection of $PGF_{2\alpha}$ or cows given a PRID for 7 days with one $PGF_{2\alpha}$ injection had a different distribution of detected heats. Cows receiving the PRID devices had a lower frequency of detected heats at less than 66 hours after $PGF_{2\alpha}$ injection. In addition, conception rate to first insemination for multiparous cows was greater with the PRID treatments than the $PGF_{2\alpha}$ given twice 14 days apart.[14] This benefit was not observed in primiparous cows. Stevenson *et al.*,[44] demonstrated that administration of a PRID for 7 days with one injection of $PGF_{2\alpha}$ 24 h prior to removal of the PRID increased the percentage of cows detected in estrus (71%) compared to a single injection of $PGF_{2\alpha}$ (44%). From a management perspective, this increased the percentage of cows that conceived during a limited synchronization period.

We now know that progesterone or progestin treatment has several physiological effects that contribute to an alteration in reproductive responses. Treatment with a progestin in the nonluteal phase of the estrous cycle will cause a lower pregnancy rate due to the development of persistent follicles with lower fertility.[38,42] In contrast, the incidence of follicle turnover is greater when a progestin is given during the luteal phase of the estrous cycle and subsequent pregnancy rates are higher. Clearly, the incidence of detected estruses is greater when cows have progesterone exposure preceding the injection of $PGF_{2\alpha}$. The shorter the progestin exposure the greater is the probability that development of a persistent dominant follicle will not occur, but potential estrous responses will be greater.

In summary, combination of progesterone or progestin treatment with $PGF_{2\alpha}$ injections offers some options to improve reproductive managment of dairy cows. Indeed, progesterone treatment is about the only option that can be applied to all cows for early re-synchronization following an initial insemination that will not disrupt an existing pregnancy. Cows[13,50] or heifers that are non-pregnant to first service can be effectively re-synchronized by progesterone treatment in the late luteal phase following insemination while the exogenous progesterone exposure will not compromise an ongoing pregnancy.

Synchronization of Ovulation and Timed Insemination

Dairy herd reproductive efficiency is commonly measured by the herd's calving interval (CI). The CI affects the pounds of milk produced per day per lifetime of cows in the herd and the income associated with these cash flows contributes to the herd's profitability.[11] The calving interval is determined by the voluntary waiting period (VWP), estrus detection rate (EDR), conception rate (CR) and abortion rate. As described earlier, cows become pregnant after the VWP as a function of the EDR and CR. Pregnancy rate (PR) is the product of these two factors (PR=EDR x CR). Pregnancy rate represents the proportion of cows that become pregnant each estrous cycle, and determines the days at which cows become pregnant after the VWP.[11] The relationship between PR and the calving to conception interval is shown in Figure 2. As the PR increases from a higher EDR, greater CR or both, the interval from calving to conception decreases.[17] Ferguson and Galligan,[11] have shown that PR to first insemination explained 79% of the variation in the CI. These authors concluded that maximizing the EDR and CR for first insemination is the most important factor influencing CI.

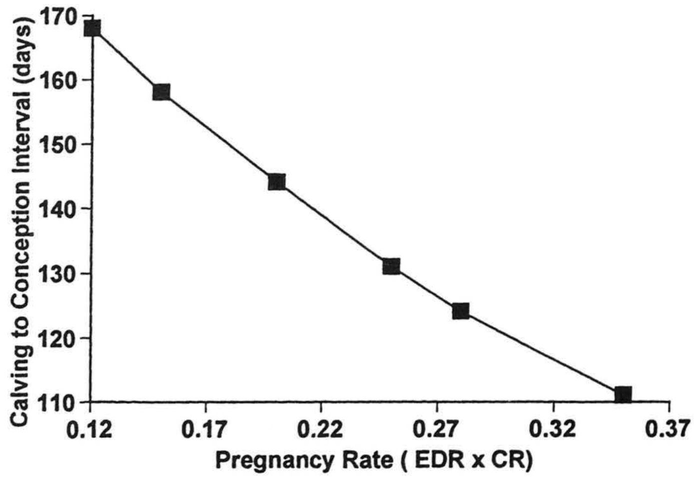


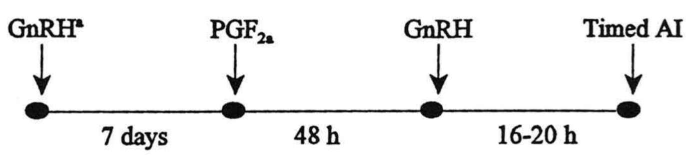
Figure 2. Effect of Pregnancy Rate (EDR x CR) on the calving to conception interval.[2]

For the most part, estrus synchronization protocols in lactating dairy cows have been limited to the use of prostaglandin $F_{2\alpha}$ or its analogues ($PGF_{2\alpha}$). However, estrus is not synchronized with sufficient precision to permit an acceptable CR based on timed insemination using $PGF_{2\alpha}$, because this treatment does not synchronize growth of follicles and the preovulatory surge of LH. Treatment with $PGF_{2\alpha}$ only regulates lifespan of the corpus luteum (CL). Therefore, detection of estrus is needed over a 7-day period after $PGF_{2\alpha}$ is administered.[21] When cows are treated twice with $PGF_{2\alpha}$ 14 days apart and artificially inseminated at a fixed time 72 to 80 hrs after the second PGF_2 treatment, CR is lower than in cows inseminated at detected estrus.[23,46] The low CR following the use of $PGF_{2\alpha}$ alone is a lack of precision between $PGF_{2\alpha}$ treatment and time of ovulation relative to insemination. Other time insemination protocols have been tested involving the induction of a LH surge following injection of $PGF_{2\alpha}$.[23,36] Injection of gonadotropin releasing hormone at 48 h after injection of $PGF_{2\alpha}$, to induce a preovulatory surge of LH, and a fixed time AI 15 h later resulted in a lower pregnancy rate compared to daily estrus detection and insemination at estrus over a 25-day period (22% vs. 36%, P<.05, 36). In cows that received GnRH at 72 h after $PGF_{2\alpha}$ and inseminated at 80 h had a lower pregnancy rate.[23] Dailey and coworkers[5] reported an increase in pregnancy rate in dairy heifers that received an injection of estradiol benzoate (400 µg) at 40 to 48 h after an injection of $PGF_{2\alpha}$ and were AI at 80 h after $PGF_{2\alpha}$ treatment. This is a promising protocol that needs to be tested in lactating dairy cows. However, at the present time injection of estradiol benzoate is not approved for use in lactating dairy cows.

Injection of gonadotropin releasing hormone or its analogues (GnRH) followed by treatment with $PGF_{2\alpha}$ 7 days later has been used effectively to synchronize estrus.[48,49,51] In contrast to synchronization with $PGF_{2\alpha}$ alone, the GnRH combined with $PGF_{2\alpha}$ treatment, takes advantage of synchronizing follicular growth and estradiol secretion with luteolysis in a sequential manner. In turn, this contributes to greater precision in timing of estrous behavior.

OVSYNCH / TAI Program

Research initiated at the University of Wisconsin has led to the development of a new timed artificial insemination program without the need for detection of estrus in lactating dairy cows.[27] Injection of GnRH can induce ovulation of a dominant follicle and when used after synchronization of follicular growth and CL regression, should program ovulation and increase the success of insemination at a fixed time.[27,35,40] This program is called the OVSYNCH protocol and is shown in Figure 3. The OVYSYNCH protocol synchronizes ovulation within an 8-h period from 24 to 32 h after the second injection of GnRH. This synchrony allows for a more successful timed artificial insemination (TAI) without the detection of estrus.[30] Because the program synchronizes ovulation and permits a TAI, it is referred to as OVYSYNCH/TAI to reflect these physiological events in this presentation.



[a]Treatment may be started on any day of the estrous cycle. Although dosages vary between GnRH analogues, their physiological responses are similar.

Figure 3. OVSYNCH/TAI protocol.

The first injection of GnRH induces release of luteinizing hormone (LH) and follicle stimulating hormone (FSH) which will ovulate or luteinize a dominant follicle, and initiate a new follicular wave. If not, it will be injected during a period of time when a new follicular wave is beginning spontaneously . Seven days later, $PGF_{2\alpha}$ injected intramuscularly should cause the regression of all CL. If a CL resulted from the initial injection of GnRH, the 7-day interval usually provides sufficient time for the CL to mature and be responsive to $PGF_{2\alpha}$. Forty-eight hours later, a second injection of GnRH should cause LH release and ovulation of a dominant follicle. The period of time between the first and second GnRH (9 d) is sufficient time for recruitment, selection and growth of a new dominant follicle to pre-ovulatory size that will be responsive to the induced surge of LH from the second GnRH treatment. The GnRH will induce ovulation in approximately 30 hrs. Cows are artificially inseminated at approximately 16-20 hrs before ovulation. The premise is that capacitated sperm will be present in the uterine tubes at the time of ovulation.

Field Studies Evaluating OVYSYNCH / TAI in Lactating Dairy Cattle

Various studies have examined conception and pregnancy rates in lactating dairy cows subjected to a OVYSYNCH/TAI program compared with those inseminated at detected estrus.[2,3,8,30,31,39,45] In these studies, conception rate was defined as the number of pregnant cows divided by the number inseminated at detected estrus. Pregnancy rate was defined as the number of pregnant cows divided by the number of cows in the study group. Because all cows in the OVYSYNCH/TAI group were inseminated on appointment, conception and pregnancy rates in the group were the same. Cows inseminated after detection of estrus had been synchronized with $PGF_{2\alpha}$ alone or in combination with GnRH at 60 to 289 days postpartum.

In a study by Stevenson and coworkers,[45] 143 lactating Holstein cows and 27 Holstein replacement heifers were assigned randomly to one of two treatments. Animals in the OVYSYNCH/ TAI group (n=85) received 100 µg of GnRH followed in 7 d by $PGF_{2\alpha}$. A second dose of GnRH (100 µg) was given 30 to 32 hrs after $PGF_{2\alpha}$ to induce ovulation of the dominant follicle, and insemination was performed 18 to 19 hrs later. Controls (n = 85) were given 25 mg of $PGF_{2\alpha}$ intramuscularly and inseminated at detected estrus. If no estrus was observed, $PGF_{2\alpha}$ was reinjected 14 d later. The pregnancy rate of heifers and cows in the OVYSYNCH/TAI group (35.3%) tended (P= 0.19) to be greater than the pregnancy rate of controls (26.5%). Furthermore, pregnancy rates of cows and heifers in the OVYSYNCH/TAI group (35.3%) did not differ signficantly from the pregnancy rate of controls (47.1%) did not differ significantly. In another study, using the OVSYNCH/TAI protocol, conception rates were not different from those of lactating cows inseminated at detected estrus.[27]

Burke and coworkers,[2] contrasted conception and pregnancy rates of primarily first lactation cows that underwent OVSYNCH/TAI with those synchronized with GnRH followed in 7 days with $PGF_{2\alpha}$ and inseminated at detected estrus. The study was conducted in Holstein cows of first (n=233) and later (n=66) lactations. All cows were treated with $PGF_{2\alpha}$ between postpartum days 27 and 33 to eliminate existing CLs and to increase the potential number of estruses prior to AI. The VWP was 75 days for cows in their first lactations and 60 days for multiparous cows. Treatment groups were synchronized by an injection of GnRH at 65 ± 3 days postpartum for primiparous cows or at 51 ± 3 d postpartum for multiparous cows, followed 7 days later with an injection of $PGF_{2\alpha}$. Forty-eight hours later cows in the OVSYNCH/TAI group (n=171) received a second injection of GnRH and were inseminated 16 h later. Cows in the control group (n=128) were inseminated at detected estrus after the $PGF_{2\alpha}$ injection. Cows that were observed in estrus prior to the injection of $PGF_{2\alpha}$ were inseminated at detected estrus (Control, n=13 [10%]; OVYSYNCH/TAI n=6[3%]). Cows in the OVSYNCH/TAI group that exhibited estrus within 40 h after the injection of $PGF_{2\alpha}$ (n=17[9%]) were inseminated. Cows in the OVSYNCH/TAI group were bred by timed AI only once at first service, subsequent inseminations occurred at detected estrus. If estrus was not detected in cows in the control group within 7 days of the $PGF_{2\alpha}$ injection, cows were subjected to a second synchronization of GnRH again at 79 ± 3 days followed 7 days later by an injection of $PGF_{2\alpha}$. Pregnancy was diagnosed by palpating the uterus and its contents per rectum at 42 days after insemination in both groups. To compare reproductive performance of cows in the synchronized control and OVSYNCH/ TAI groups with a less intensive reproductive program, a more conventionally farm-managed group also was evaluated. In that group, cows received periodic $PGF_{2\alpha}$ treatment postpartum. That group was comprised of cows in their first lactation (n=250) that calved within 45 days before initiation of the experimental control and OVSYNCH/TAI groups. Those cows were maintained under conditions similar to those for cows in the designed experiment.

Pregnancy rate was 30.5% for cows in the Control group during d 1 to 6 of AI after $PGF_{2\alpha}$ injection and 29% for cows in the OVSYNCH/TAI group. Pregnancy rates for cows in the OVSYNCH/TAI group were relatively stable at approximately 30% from January to April. Pregnancy rates decreased to 22% in May. Pregnancy rates of cows in the Control group were much more variable from month to month, varying from a high of 62% during January to a low of approximately 12% during April and May (Figure 4A). Similarly, the effect of the reproductive program on conception rate was influenced by month (Figure 4B). Rate of estrus detection was greater for first synchronization (67.2%) than second synchronization (45.6%). Consequently, pregnancy rate was lower for those control cows synchronized a second time (10.8% vs 30.2%), whereas conception rate was not different (37%) between first and second synchrony. The overall pregnancy rate by 120 days postpartum was not different between cows in the Control (58.8%) and OVSYNCH/TAI (56.2%) groups. The calving to conception interval for those cows that conceived by 120 days postpartum was reduced ($P < .07$) in cows in the OVSYNCH/TAI group (79.0 days) compared with cows in the Control group (83.7 days). Number of days to first insemination was reduced by 8.1 days postpartum in first lactation cows managed in the OVSYNCH/TAI group and 6.1 days postpartum in multiparous cows managed in the OVSYNCH/TAI group compared with cows in the Control group ($P < .01$). For the cows in the farm management group, estrus detection rate was 74.0% and first insemination occurred between 13 and 82 days postpartum.

This study demonstrated that a OVSYNCH/TAI program involving the use of GnRH could eliminate the need for estrus detection and protect against negative factors affecting reproductive efficiency because pregnancy and conception rates were more consistent

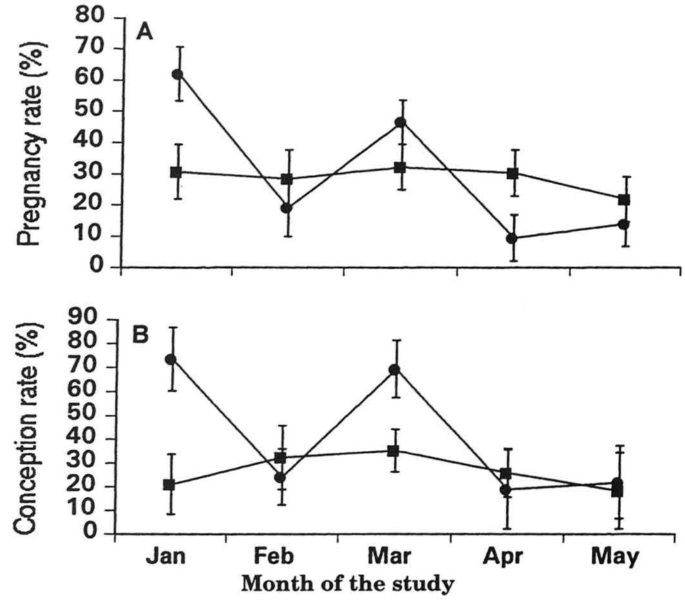


Figure 4. (A) First AI pregnancy rate (percentage) at first synchronization adjusted for treatment, lactation, and month for cows inseminated at detected estrus (Control; ●; n - 128) or timed AI (TI; ■; n = 171). The cows in the TI grop that were inseminted before the second injection of GnRH agonist (n = 17) were considered nonpregnant. The least squares means are presented for each month January through May.
(B) First AI conception rate (percentage) at first synchronization adjusted for treatment, lactation, month, technician, and semen source for cows inseminated at detected estrus (●; n = 85) or TI (■; n = 171). The least squares means are presented for each month January through May.[12]

from month to month for cows in the OVSYNCH/TAI group. Pregnancy rate and conception rates were not different between control cows and cows managed in the Ovsynch/TAI group. Estrus detection was not necessary within the OVSYNCH/TAI system, except for the few cows (10%) that were observed in estrus before the designated breeding date. The use of OVSYNCH/TAI provided a greater control of reproductive management than the farm's estrus detection practices. For example, some cows were inseminated for the first time too early postpartum (13 days) or too late (82 days). Although estrus detection rate did not differ from month to month, other management factors could have contributed to the decline in pregnancy rate in cows inseminated at detected estrus during February, April, and May. These include insemination of cows that were not truly in estrus. This can occur in cows inseminated at detected estrus, but would not occur in cows managed with OVSYNCH/TAI. The value of a OVSYNCH/TAI program likely increases significantly in a situation of spurious estrus detection practices.

Pursley and coworkers[31] evaluated pregnancy rates obtained by OVSYNCH/TAI compared with those after a synchronization program using repeated $PGF_{2\alpha}$ injections and insemination after detection of estrus (Controls) in lactating dairy cows (n=310) and heifers (n=155). The lactating dairy cows, 60 to 289 d postpartum, and heifers were assigned randomly to two groups. Cows in the Control group received up to three i.m. injections of $PGF_{2\alpha}$ 14 d apart. Only those cows not detected in estrus were given subsequent injections of $PGF_{2\alpha}$. Cows detected in estrus after $PGF_{2\alpha}$ injection were inseminated using the AM- PM rule. All Controls not detected in estrus after the third injection of $PGF_{2\alpha}$ received one fixed-time AI at 72 to 80 hrs after the $PGF_{2\alpha}$ treatment. Cows in the OVSYNCH/TAI group received the treatment sequence shown in Figure 3. However, the second GnRH treatment was given 30 to 36 hrs after the $PGF_{2\alpha}$ treatment. Pregnancy diagnosis was determined by ultrasound 25 to 30 days after breeding on 80% of the cows and heifers and by rectal palpation between 35 to 49 days following AI on 20% of the cows and heifers. Pregnancy rate per AI was defined as the percentage of cows or heifers that were confirmed pregnant at the single pregnancy diagnosis (ultrasound or palpation) after one AI for the OVSYNCH/TAI group. In the control group pregnancy rate evaluation included cows inseminated after one to two $PGF_{2\alpha}$ injections as well as a timed insemination at 72-80 after a third $PGF_{2\alpha}$ treatment in cows not detected in estrus. The OVSYNCH/TAI protocol resulted in a pregnancy rate per AI that was similar to the rate for cows receiving $PGF_{2\alpha}$ every other week and inseminated at detected estrus (38.9 vs 37.8, P > .10). Of those cows bred by a timed insemination after the third $PGF_{2\alpha}$ injection in the control grou, only 8.3% conceived .

Another study by Pursley *et al.*,[28] examined whether OVSYNCH/TAI could be an effective method to manage reproduction in lactating dairy cows compared with daily detection of estrus and the a.m.-p.m. breeding rule. Lactating dairy cows (n=333) from three herds were assigned at parturition to a control or a OVSYNCH/TAI group. Control cows were managed according to the typical reproductive statregy of the farm that relied on detection of estrus, the a.m.-p.m. breeding rule, and periodic use of $PGF_{2\alpha}$. Cows in the OVSYNCH/TAI followed the OVSYNCH/TAI protocol shown in Figure 3. The VWP was 50 days postpartum, and the OVSYNCH/TAI protocol was initiated 40 to 48 days postpartum. Pregnancy diagnoses were performed for cows in both groups by ultrasound between 32 and 38 days after insemination. Pregnancy was confirmed by ultrasound detection of a fetal heart beat. If the ultrasonographer was unsure of the pregnancy, the cows were re-evaluated 1 week later. Nonpregnant cows were inseminated again using the original treatment protocol (OVSYNCH/TAI) until diagnosed as pregnant or until culled from the herd. Days to first insemination (54 vs 83, P<.01) and days open (99 vs 118, P<.05) were lower for treated cows than for control cows, respectively. Pregnancy rates for each AI were defined as the number of cows pregnant at 32 to 38 days after AI divided by the total number of cows that received that AI. Pregnancy rate for first AI were similar (37% vs 39%) for both groups. More cows in the OVSYNCH/TAI group than control cows were pregnant at 60 days (37% vs. 5%, P<.01) and at 100 days (53% vs. 35%, P<.01) after calving. The authors concluded that this protocol allowed effective management of AI in lactating dairy cows without the need for estrus detection. Retreatment of cows diagnosed not pregnant allowed for a re-insemination without the need for detection of estrus. In essence, the need for heat detection was potentially eliminated based on the use of OVSYNCH/TAI for re-insemination.

Management Factors that Affect OVYSYNCH / TAI

There are several management factors that can affect success of the OVSYNCH/TAI program and need to be investigated to improve pregnancy rate. In most of the studies cited above, the OVSYNCH/TAI program was performed only for first insemination. As shown by Pursley *et al.*,[28] ultrasound at 32 to 38 days post insemination can be used effectively to determine pregnancy status, allowing re-synchronization of non-pregnant cows for subsequent insemination. Several situations develop during the OVSYNCH/TAI protocol that impact on decisions for the producer. At the time of $PGF_{2\alpha}$ injection and during the next 36 h approximately 10% of cows will express estrus. These cows should be inseminated at detected estrus and do not need to receive the second injection of GnRH. In our experience these cows are at approximately day 14 to 15 of the estrous cycle at the time of the first GnRH injection and fail to produce a CL in response to GnRH. Thus, in 7 days, at the time of $PGF_{2\alpha}$ injection, they are in estrus and should be inseminated.

Another common question concerns the timing of AI following the second injection of GnRH given 2 days after the injection of $PGF_{2\alpha}$. Cows will ovulate 28 to 30 hours after the injection of the second GnRH of OVSYNCH/TAI, and they should be inseminated 15 h prior to ovulation to allow semen to undergo capacitation in order to fertilize the egg following ovulation. A University of Wisconsin study[29] evaluated the conception rate of inseminations at 0 h (37%), 8 h (40%), 16 h (44%), 24 h (40%) and 32 h (32%) after injection of GnRH. Pregnancy rate was maximal at 16 h. However, a surprising percentage of the cows were pregnant when inseminated at the time of GnRH injection (0 h) and close to the time of ovulation (32 h). However, pregnancy rate was reduced signficantly at 32 h. Thus, alternative insemination times are possible. It is anticipated that maximal pregnancy rates will be obtained between 8 and 24 h or at 16 h after GnRH injection.

Figure 5 shows a significant relationship of increased pregnancy rates with increases in body condition score (BCS) of the cow.[2] Figure 5 shows that cows with higher BCS at OVYSYNCH/ TAI had higher pregnancy rates. Cows suffering from postpartum anestrus (progesterone concentration < 1 ng/ml for 60 days postpartum) are known to eat less feed, produce less milk, and lose more body weight, resulting in a more negative energy status than cycling cows.[43] Cows that were not cycling (true anestrus) did not have improved reproductive performance when treated with GnRH over untreated controls that were also anestrus.[6,18] Therefore, cows that are not cycling should not be expected to have a normal response rate to the OVSYNCH/TAI protocol.

Our field experiments with OVSYNCH/TAI indicate a lower fertility rate in cows identified to be in anestrus. With our ability to guarantee that all cows can be inseminated precisely at a designated time postpartum with the use of OVSYNCH/TAI, producers can lengthen the VWP, since the time of first insemination is controlled more precisely. If all cows are cycling, a normal program of inseminating at detected estrus, assuming a 50% estrus detection rate, would have to be started at day 40 to ensure that the mean time of insemination will be day 70 (range 40-100 days). However, an OVSYNCH/TAI program permits all inseminations to be made at 70 $\pm$ 3 days if implemented on a weekly basis. Furthermore, pregnancy rates for cows that underwent OVSYNCH/TAI between 76-100 days postpartum were greater than cows that received OVSYNCH/TAI between 50-75 days (47% vs. 35% ; 29). Thus, it may be an advantage to delay first inseminations until a period of greater fertility, using the OVSYNCH/TAI program to ensure that there will be no net loss in time to first service by controlling the time of insemination for all cows.

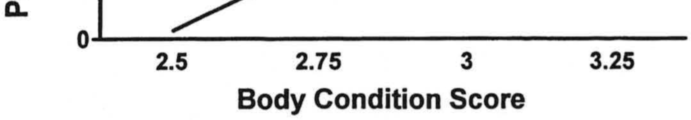


Figure 5. Relationship between pregnancy rate and body condition score in lactating dairy cows.[23]

Timed Artificial Insemination in Heifers

In heifers, the use of the OVYSYNCH/TAI program insemination has not improved conception rates when compared to insemination at detected estrus.[31,39] Heifers assigned to a OVYSYNCH/TAI treatment (Figure 3) had similar pregnancy rates but lower conception rates when compared to heifers inseminated at detected estrus. Replacing the second injection of GnRH agonist (Buserelin) with an injection of hCG (3,000 IU) resulted in comparable pregnancy rates when compared to controls, but did not prevent a reduction in conception rate. However, the frequency of shortened interestrus intervals was reduced in hCG treated heifers.[39]

Pregnancy rates were almost twice as great for heifers inseminated at detected estruses following a $PGF_{2\alpha}$ reproductive management program compared with heifers inseminated at one fixed time using the OVSYNCH/TAI protocol.[31] It should be emphasized that in this study, heifers in the control group received up to three i.m. injections of $PGF_{2\alpha}$ 14 days apart and were inseminated following the AM-PM rule when detected in estrus. All control heifers not detected in estrus after the third $PGF_{2\alpha}$ injection received one fixed-time AI at 72 to 80 hrs after the $PGF_{2\alpha}$ treatment. An alternative presentation of the data is to examine the pregnancy rate of all heifers that received the single first injection of $PGF_{2\alpha}$ (e.g., heifers pregnant to insemination following the first $PGF_{2\alpha}$ injection/total heifers injected with $PGF_{2\alpha}$). This analysis shows no difference (28.2% vs 35.1%; P > .10) in pregnancy rates between Control vs OVSYNCH/TAI, respectively. Nevertheless, differences in follicular dynamics between heifers and cows may affect the response to the OVSYNCH/TAI program.

Use of OVYSYNCH / TAI in Lactating Dairy Cattle During Periods of Heat Stress

Pregnancy rate, which is a product of estrus detection and conception rates, is reduced during seasonal periods of heat stress. Heat stress reduces plasma estradiol during proestrus and lowers estrus detection rates.[6] Conception rates also are reduced during heat stress due to elevations in body temperature that result in early embryonic death.[32] De la Sota *et al.*,[8] compared the efficiency of a reproductive management program involving the OVSYNCH/TAI program with a typical farm management program involving $PGF_{2\alpha}$ treatment alone in which cows were inseminated at detected estrus, under heat stress conditions in Florida. The hypothesis was that because OVSYNCH/TAI increases estrus detection rate to 100% (all cows are inseminated), the pregnancy rate should increase. The study[8] was conducted from May to September with primiparous (n=133) and multiparous (n = 71) lactating Holstein cows. At 30 ± 3 days postpartum, all cows were injected with $PGF_{2\alpha}$ to regress any existing CL. The VWP was set at 60 d postpartum. Timed inseminated cows (n=148) were synchronized using the OVSYNCH/TAI protocol shown in Figure 3. Cows in the control group (n=156) were injected with $PGF_{2\alpha}$ at 57±3 days postpartum and inseminated when detected in estrus. All cows in both groups were re-inseminated at subsequent detected estruses. First inseminations occurred from May through September, 1995. Pregnancy rate was greater for OVSYNCH/TAI-managed cows than cows of the control group (13.9 vs. 4.8%, P<.05). Pregnancy rate for all cows varied from month to month, ranging from a low of 4.5 ± 5% in June to a high of 20.0 ± 3.7 % in July for all cows (P<.05). No treatment by month interaction was detected. The proportion of cows detected in estrus and inseminated during days 1 to 6 after injection of $PGF_{2\alpha}$ was only 18.1% for control cows, compared to an insemination rate of 100% for OVSYNCH/TAI cows. The interval between $PGF_{2\alpha}$ injection and insemination was 35.5 days for control cows compared with only 3.0 days for OVSYNCH/TAI cows (P<.05). This interval tended to decline from May (49.2 ± 4.3) to September (21.7 ± 3.8) for control cows. Likewise, number of days postpartum to the first insemination was less in OVSYNCH/TAI than in control cows (58.7 vs. 91.0 days, P<.05). This response tended to decline from May (104.7 ± 4.4 days) to September (78.0 ± 3.8) in control cows, but did not change in OVYSYNCH/TAI-managed cows. The longer interval from $PGF_{2\alpha}$ injection to insemination for the control group reflects summer time reduction in detection of heats that was eliminated with OVSYNCH/TAI. Conception rate for control cows detected in estrus and inseminated was greater (25.9%) than cows of the OVSYNCH/TAI group (13.2%, P<.05). However, this increase in conception rate is misleading since only 18% of the control cows were detected in estrus and inseminated, whereas all of the OVSYNCH/TAI cows were inseminated. The overall pregnancy rate by 120 days postpartum was greater for OVSYNCH/TAI cows when compared with control (27.0 vs.16.5%, P<.05). Number of days open for cows that conceived by 120 days postpartum was 12.4 days less for OVSYNCH/TAI compared with control-managed cows (77.6 vs.90.0, P<.05).

As expected, pregnancy rate was significantly higher for the OVYSYNCH/TAI group because of the higher number of cows inseminated. The OVYSYNCH/TAI management program will not protect the embryo from temperature-induced embryonic death, but limitations induced by heat stress on detection of estrus are eliminated. For all cows that did conceive, days open were reduced by 12.4 days and the percentage of cows pregnant by 120 days postpartum was increased for the OVYSYNCH/TAI group.

Economics of OVYSYNCH/TAI in Dairy Cattle

Pregnancy rate may be defined as the product of estrus detection and conception rate (PR = EDR x CR; 3). As PR increases from a higher EDR, CR or both, the interval from calving to conception decreases.[17] A reduction in the calving to conception interval results in an increase in the pounds of milk produced per day per herd lifetime and a reduction in cows culled for reproductive failure.[33] In reality, the exact net revenues depend on the individual farm circumstances, but Figure 6 is based on a widely-representative farm scenario. Improvements in PR beyond 25% result in smaller incremental increases in net revenue, and virtually no increase in net revenue is experienced beyond a PR of 35%. The OVYSYNCH/TAI protocol is a reproductive management tool in which a virtual EDR of 100% is implemented. For a dairy herd with a 60%

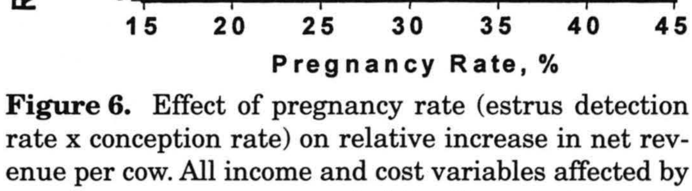


Figure 6. Effect of pregnancy rate (estrus detection rate x conception rate) on relative increase in net revenue per cow. All income and cost variables affected by pregnancy rates are accounted for. These include milk produced, feed costs, reproductive culling, replacement costs and other variable costs.

EDR and a 30% CR in a given period, herd PR will be 18%. Implementation of OVYSYNCH/TAI to achieve a 100% EDR has the potential to increase herd PR to 30%. Figure 2 demonstrates that the effect of OVYSYNCH/TAI can be a major incremental increase in net revenue per cow.

In order to estimate the economical impact of OVYSYNCH/TAI we have used two strategies. The first was a direct approach based on experimental data in which costs per cow associated with control (insemination at detected estrus; n=148) and OVYSYNCH/TAI (n=156) reproductive management were calculated from a heat stress experiment.[8] The reproductive performance of each cow was followed for a 365-day period. Since reproductive costs were the only source of variation in the economic returns between the control and OVYSYNCH/TAI groups, advantage for either group from reproductive performance was considered a net revenue gain. Cumulative pregnancy rates for the two groups are depicted in Figure 7. There was an immediate increase in PR due to the OVYSYNCH/TAI and a second increase in PR in cows that did not conceive to first service but had a spontaneously synchronized service at approximately 21 days after the OVYSYNCH/TAI. This difference in PR for OVYSYNCH/TAI treated cows appeared to be maintained throughout the 365-day period. Cows in the OVYSYNCH/TAI group had a greater percentage of pregnant cows by 365 days (87% vs. 77.9%; P<.05), 22 less days open (153.2 vs. 175.7 days; P<.01), and 9% less cows culled due to reproductive failure (12.9% vs 22.0%; P<.05). Days open were calculated for all cows (pregnant and open) in the experiment. Cows that did not conceive by the end of the experiment were considered to have 365 days open or respective days open at time of culling.

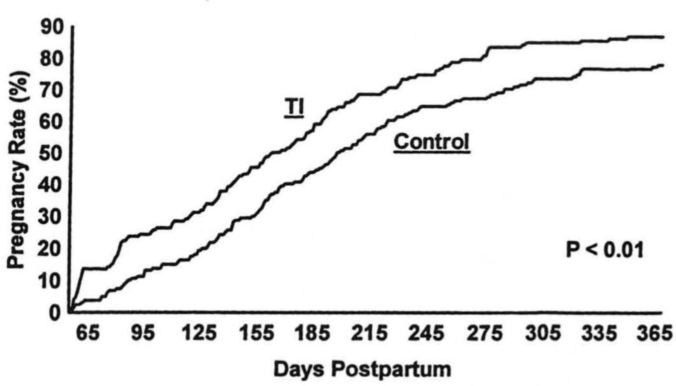


Figure 7. Cumulative frequency of pregnancy rates (the occurrence of pregnancy for experimental cows was cumulated throughout a 365 day period) in lactating dairy cows that received their first postpartum service in summer as an OVYSYNCH/TAI or at a detected estrus in control cows that received a single injection of $PGF_{2\alpha}$.

To achieve the greater pregnancy rate at first service with OVYSYNCH/TAI (13.9 vs. 4.8%; P<.05), an appreciably greater number of services was made compared to the control group. This contributed to a greater number of services per conception by 120 days postpartum for the OVYSYNCH/TAI group (1.63 vs. 1.27; P<.05). However, by 365 days postpartum number of services per conception was the same (3.76 OVYSYNCH/TAI and 3.52 control). A greater number or proportion of control cows needed to be inseminated through the remaining 365-day period. This led to an equal number of services per conception and a smaller proportion of cows pregnant by 365 days. Furthermore, the total number of services per cow (pregnant and open) through 365 days did not differ (3.87 OVYSYNCH/TAI vs.3.72 control).

Estimated total costs for reproductive management of OVYSYNCH/TAI and control cows during the summer heat stress experiment were determined.[8] The following costs were utilized: $3.00/injection dose of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), $6.00 per dose of gonadotrophin-releasing hormone (GnRH), $7.00 per straw of semen, $2.14 cost per day open after 60 days, a cull cost of $900 as the differential value of a replacement heifer minus salvage value of the culled cow, and a labor cost of $0.50 per injection. The cost of $2.14 per day open after 60 days was obtained from a previously published report.[47] With these costs, total costs for the two groups are summarized in Table 1. The total costs for the OVYSYNCH/TAI group were $53,066 or $359.00 per cow compared to costs of the control group of $75,284 or $476 per cow. This results in a cost reduction or an increase in net revenue of $118 per cow that was managed with OVYSYNCH/TAI at first service compared to control cows which were synchronized with a single $PGF_{2\alpha}$ injection.

Our second analytical approach was to contrast net revenue of the OVYSYNCH/TAI program during summer with the concurrent control group (periodic use of $PGF_{2\alpha}$ and insemination at detected estrus) utilizing an economic modeling program which accounts for alterations in management practices to maximize the net revenue while considering other herd performance measures. DeLorenzo *et al.*[9,10] used dynamic programming to determine profit maximizing, insemination and culling practices considering both production and financial variables. The model responds to the production and cost data from the specific dairies, but exogenous cost variables are representative of the entire industry. Inputs include lactation curves, heat detection rates, conception rates, seasonal breeding performance, seasonal milk production, seasonal milk prices, and feed and other costs related to production and income. The model can compare a status quo current herd forecast for 12 months to a forecast

Table 1. Differences in costs associated with control versus OVYSYNCH/TAI during a 365-day period with first experimental service in summer[a].

Costs	Control[b]	OVYSYNCH/TAI[c]
Number of cows	148	156
Drugs[d]	$468.00	$2,220.00
Semen[e]	$4,062.24	$4,009.32
Labor[f]	$78.00	$222.00
Days open[g]	$38,625.29	$29,518.30
Replacements[h]	$31,050.00	$17,100.00
Total costs	$74,283.53	$53,069.62
Total cost per cow	$476.18	$358.58
Difference per cow		$-117.60

[a] De la Sota *et al.*[8]

[b] Artificial Inseminations made to detected estrus following an injection of $PGF_{2\alpha}$ in summer.

[c] Timed artificial insemination to first service using the protocol sited in Figure 3.

[d] Drugs: $3 per control cow and $15 per OVSYNCH/TAI cow.

[e] Semen: $7 x $3.72 services per control cow x 156 control cows; $7 x 3.88 services per OVSYNCH/TAI cow x 148 OVSYNCH/TAI cows.

[f] Labor: $0.50 per control cow and $1.50 per OVSYNCH/TAI cow.

[g] Days open: $2.14 x 115.7 days open x 156 control cows; $2.14 x 93.2 days open x 148 OVYSYNCH/TAI cows.

[h] Replacements: $900 x 34.5 cows culled for being open in the control group; 900 x 19 culled open cows in OVTSYNCH/TAI group.

assuming optimal policies are followed for breeding and culling. Such a modeling program provides descriptive information regarding herd performance, diagnostic information which may help determine when profitability and herd performance are not optimized, the financial effect of implementation of a new technology or production opportunity, and prescriptive information suggesting profit-maximizing breeding and culling strategies. This approach provides an opportunity to evaluate the impact of new production technology, such as OVYSYNCH/TAI, considering interactions with other productive and economic variables not available by other methods.

We developed several OVYSYNCH/TAI management scenarios, utilizing field reproductive responses (EDR, CR and PR) from the study by Burke *et al.*[2] and estimated their impacts on net revenue per cow within the herd utilizing the economic modeling program. Utilizing this modeling approach, we evaluated the effect of OVYSYNCH/TAI for first service during the summer compared with the $PGF_{2\alpha}$-treated control group for EDR, CR and PR as described by De la Sota *et al.*[8] Experimental field results were collected from the same dairy in consecutive seasons (January to May [2] and June to September [8]). Economical analyses were made from specific inputs characteristic of the dairy. The following assumptions were made for inputs for the dairy in which the summer heat stress experiment was performed: net milk price, $15 per 100 pounds; average mature equivalent for milk production of 23,500 pounds; ration cost for lactating cows of $0.08 per pound of dry matter; feed cost for dry cows of $ 1.00 per cow per day, cost of a replacement heifer of $1300, and a salvage price for cull cows of $0.30 per pound of body weight.[8] These are realistic numbers from actual farm records. The program calculated the net revenue per cow for a 1000-cow herd managed over a 12-month period in which optimal management decisions are made to maximize profit. This was done with estrus detection rates and conception rates set to each experimental reproductive management system (OVYSYNCH/TAI vs control [$PGF_{2\alpha}$ injection and inseminate at detected estrus]).

We utilized an estrus detection rate of 100% and a conception rate of 13.2% for a timed insemination to first services between June and October (hot season).[8] For the remaining 7 months (November through May; cool season), estrus detection and conception rates were those from the actual farm as determined from their DHIA records (51% estrus detection and 37% conception rates). This scenario examines the effect of implementing the OVYSYNCH/TAI reproductive management in the summer on reproductive performance for the herd year. For comparison the control scenario for the herd involved normally low estrus detection and conception rates of 18.1% and 22.9%, respectively, for first service of the summer season ($PGF_{2\alpha}$ injected control group) and those described above for the cool season, as determined from DHIA records. All subsequent services utilized estrus detection and conception rates determined from DHIA records of the farm for cool and hot seasons. Thus, the only difference associated with estimates of net revenue between these two scenarios was that attributable to an OVYSYNCH/TAI at first service in summer. The dairy modeling program estimated a $17.24 increase in net revenue per cow by implementing the OVYSYNCH/TAI management system in the summer for first service compared to the herd control scenario. These predicted differences in net revenue were compared to actual calculated differences in net revenues (Table 2) for experimental cows of the OVYSYNCH/TAI versus control that were determined in[8] and presented in Table 1. A major difference in estimates of net revenues is due to estimates in replacement costs. In the modeling comparisons to examine the impact of OVYSYNCH/TAI in summer on optimal herd performances for the year, there was no difference in culling rate. However, the direct estimate for only the experimental cows detected a difference in culling rate between OVYSYNCH/TAI versus control for first service in summer which

Table 2. Comparison in net revenue obtained by direct calculation from experimental cows or by utilizing the dairy modeling program.

Response	Data from OVYSYNCH/TAI trial during summer[a]	Dairy modeling program[b]
Differences in net revenues	$ 117.93	$17.24
- replacement	$70.76	$0
- days open	$47.17	$17.24
Differences in semen cost	$1.05	$4.75
Differences in semen cost	$1.05	$4.75
Cost per day open	$2.14 (22.5 d open)	$1.16 (18.0 d open)

[a] From De la Sota *et al.*[8]
[b] From DeLorenzo *et al.*[9,10]

enhanced net revenue by $70.76 for OVYSYNCH/TAI-managed cows (Table 2). Both analytical approaches approximated the same reduction in days open of approximately 20.2 days (Table 2). The differences in net revenue associated with days open ($47.17 versus $17.24) is accounted for by a greater semen cost per cow and a lower cost per day open for the dairy modeling program. Both estimates of net revenue have been adjusted for costs of drugs, semen, labor, etc. We might expect the "modeling approach" to show less difference in net revenue between management groups (OVYSYNCH/TAI versus control in summer), because it does the best possible with each set of biological performances for each group. Regardless of the estimate, use of OVYSYNCH/TAI for first service resulted in substantial increases in net revenue per cow.

Utilizing the data bases generated from our field experiments,[2,8] we are able to develop multiple scenarios involving implementation of the OVYSYNCH/TAI reproductive management system under seasonal conditions of Florida. The year was divided into two seasons: the cool (November through May) and hot (June through October) seasons. The decision to not artificially inseminate (AI) cows in the summer was evaluated along with the effects of implementing OVYSYNCH/TAI in the cool season (100% estrus detection and 31% conception rate [2]) or hot season (100% heat detection and 13% conception rate[8] or combinations of OVYSYNCH/TAI during both seasons. The insemination at detected estrus (IDE) category is use of estrous synchronization systems for first service inseminations made at detected estrus (e.g., following synchronization with GnRH and $PGF_{2\alpha}$ given 7 days apart in the cool season with estrus detection and conception rates of 67.2% and 37.9 % for the cool season,[2] or following an injection of $PGF_{2\alpha}$ in summer with estrus detection and conception rates of 18.1% and 22.9% for the hot season.[8] An additional scenario is to evaluate the use of OVYSYNCH/TAI for all cows at any service number in April just before the hot season to increase number of pregnant cows prior to the period of reduced fertility associated with heat stress. The control scenarios for cool and hot seasons are estrus detection and conception rates for the respective months determined from the herd's DHIA records (e.g., cool season: 51.0% and 37.0%; hot season, 18.0% and 18.0%, estrus and conception rates, respectively). The differences in net return associated with the various scenarios are presented in Table 3.

Table 3. Comparison of differences in net revenues per cow utilizing various reproductive management scenarios involving timed insemination.

SCENARIOS Cool Season	Hot season	Differences in net revenue per treated cow ($)
Control	Control	0
Control	No AI	-30.24
Control	OVYSYNCH/TAI	25.36
OVYSYNCH/TAI	Control	15.34
OVYSYNCH/TAI	OVYSYNCH/TAI	16.57
Control	IDE	8.12
IDE	Control	0.48
Control + OVYSYNCH/TAI APR	Control	71.35
Control + OVYSYNCH/TAI APR	OVYSYNCH/TAI	63.39
OVYSYNCH/TAI + OVYSYNCH/TAI APR	Control	31.44
OVYSYNCH/TAI + OVYSYNCH/TAI APR	OVYSYNCH/TAI	30.79

Control: conception and estrus detection rates for respective months determined from the herd's DHIA records (e.g., Cool season: 51.0% and 37.0%; Hot season, 18.0% and 18.0%, estrus and conception rates, respectively).
No AI: no artificial insemination during the hot season.
OVYSYNCH/TAI: timed artificial insemination to first service using the protocol in Figure 3.
IDE: inseminations made to detected estrus following an injection of $PGF_{2\alpha}$ or following synchronization with GnRH and $PGF_{2\alpha}$ given 7 days apart.
OVYSYNCH/TAI APR: timed artificial insemination for all cows at any service number in April prior to the hot season.

The results in net revenue show several interesting points. First, utilizing the dairy modeling program, the decision not to AI cows during the summer months is a bad decision since net revenue per cow decreased by approximately $30.00. In addition, we concluded that, independent of season of the year, OVYSYNCH/TAI was always more profitable in comparison to the control and IDE scenarios. Use of OVYSYNCH/TAI in summer for first service increased net revenue by $25.36 per cow. Implementation of OVYSYNCH/TAI in the cool season alone for first service increased net revenue by $15.34 per cow. Use of OVYSYNCH/TAI in summer months had a greater impact on net returns than the use of OVYSYNCH/TAI during the cool season. This difference can be explained by the fact that the value of increased reproductive efficiency is greater under situations when fertility rates are low, as depicted in Figure 6. Furthermore, highest values in net revenue were related to the use of OVYSYNCH/TAI for all cows open in April, independently of service number ($71.35 per cow). Our explanation for such results are based on the fact that this particular dairy has a tendency to increase its profits if calvings are concentrated in the winter season. Seasonal factors driving these results are not unique to this dairy but most dairies in Florida under good management. Also, there will be a reduced number of cows inseminated in summer at a lower fertility rate. The seasonality effect of having increased pregnancy rates in April by using OVYSYNCH/TAI results in increased profit estimates. The combination of OVYSYNCH/TAI for all cows open in April followed by OVYSYNCH/TAI to first service during the hot season increased net revenue per cow by $63.39.

Application of a synchronization program (IDE) in the cool season only increased net revenue per cow by $0.48. This reflects a lower EDR (67.2%) compared to an 100% EDR for OVYSYNCH/ TAI in the cool season and a net revenue of $15.32 per cow. Application of OVYSYNCH/TAI for all first services in both the cool and hot season increased net revenue by $16.57 per cow.

Britt and Gaska[1] compared pregnancy rates and economic benefits between the OVYSYNCH/TAI and a reproductive management program based upon injection of $PGF_{2\alpha}$ after palpation of a corpus luteum and insemination of cows at detected estrus. Insemination rates and pregnancy rates were improved significantly for cows in the OVYSYNCH/TAI group. A comparison of costs for hormonal treatments, semen and labor for both groups and the benefit of a reduction of 10.5 days for the calving to conception interval for the OVYSYNCH/TAI group resulted in an economic advantage of $29.14 per pregnancy for the OVYSYNCH/TAI group.

The most important message from these results is that OVYSYNCH/TAI may be a profitable alternative for managing large commercial dairy herds where estrus detection rates are usually less than optimal. There are still some questions left to be answered, though. We believe that achieving a 12-13 month calving interval should not necessarily be the main concern of dairy producers. Cows with different production levels and calving at different times during the year may have different optimal calving intervals. The use of OVYSYNCH/TAI would allow a more precise control of when cows become pregnant and thus calve to take advantage of variation in prices and seasonal constraints to production. In addition, there seems to be a reduction in labor costs associated with OVYSYNCH/TAI that were not considered in the estimates we presented. Although cows have to be injected three times according to the OVYSYNCH/TAI protocol, there is no labor involving estrus detection for first services. That may constitute an additional revenue source for the OVYSYNCH/TAI-managed cows. Following OVYSYNCH/TAI, cows that do not conceive have to be detected in heat in order to be re-inseminated. Further research is needed to develop re-synchronization systems that would allow cows to be OVYSYNCH/TAI continuously. A re-synchronization system that is able to produce appreciable pregnancy rates may lead to the complete elimination of heat detection in dairy herds. It is noteworthy that Pursley *et al.*[28] demonstrated the applicability of a re-synchronization OVYSYNCH/TAI program.

Additional research will further develop the OVYSYNCH/TAI system so that a greater percentage of animals will respond to the synchronization of ovulation resulting in greater pregnancy rate. Utilizing the OVYSYNCH/TAI model, potential alterations to optimize development of the corpus luteum and regulation of follicle development after insemination are possible such that pregnancy rate may be further increased. The OVYSYNCH/TAI program provides the producer with a reproductive management option to effectively implement first service at the voluntary waiting period chosen by the producer. This alone offers considerable management advantages relative to optimizing nutritional, lactational and reproductive programs.

The approach used in this presentation provides a realistic assessment of OVYSYNCH/TAI as a new reproductive technology. Any new management technique, technology, or therapy must be evaluated in realistic scenarios with all their complexities involving interactions between management skills, milk production, reproduction, prices and costs. Seasonality in most parts of the USA further complicates these interactions. It is indisputable that all technologies do not have a common value and best use across all dairies. The modeling approach used in this research provides a realistic assessment of factors affecting the value of OVYSYNCH/TAI unavailable from other approaches. Scenarios used in this study are representative of a broad range of dairies subject to summer heat stress.

An OVYSYNCH/TAI reproductive management program offers the producer the following options of application in the future that warrant investigation:

1. Delay the voluntary waiting period to restore body condition without altering days to first service for the group;

2. Precisely control time of first insemination during times of the year to maximize profit (i.e., having the majority of cows calve during fall);

3. Integrate first service in a timely manner to complement potential bovine growth hormone treatment;

4. Effectively implement a delayed breeding program if practiced with administration of bovine growth hormone;

5. Maximize pregnancy rate (EDR x CR) to first service and consequently reduce the calving to conception interval.

References

1. Britt, J.S. and J. Gaska. 1998. Food Animal Economics: Comparison of two estrus synchronization programs in a large, confinement-housed dairy herd. *JAVMA* 212: 210. 2. Burke J.M., R.L. De la Sota, C.A. Risco, C.R. Staples, E. J-P Schmitt and W.W. Thatcher. 1996. Evaluation of timed insemination using a Gonadotropin-Releasing Hormone agonist in lactating dairy cows. *J. Dairy Sci.* 79:1385. 3. Burke, J.M., C.R. Staples, C.A. Risco, R.L. de la Sota, and W.W. Thatcher. 1997. Effect of ruminant grade menhaden fish meal on reproductive and productive performance of lactating dairy cows. *J. Dairy Sci.* 80: 3386. 4. Butler W.R. and R.D. Smith. 1989. Interrelationships between energy balance on postpartum reproductive function in dairy cattle. *J. Dairy Sci.* 72: 767. 5. Dailey, R.A., R.E. James, E.K. Inskeep, and S.P. Washburn. 1986. Synchronization of estrus in dairy heifers with prostaglandin $F_{2\alpha}$ with or without estradiol benzoate. *J. Dairy Sci.*69: 1110. 6. Daily R.A., E.K. Inskeep, S.P.Washburn and J.C. Price. 1983. Use of Prostaglandin $F_{2\alpha}$ or Gonadotropin Releasing Hormone in treating problem breeding cows. *J. Dairy Sci.* , 66:1721. 7. De la Sota, R.L., M.C. Lucy, C.R. Staples and W.W. Thatcher. 1993. Effects of recombinant bovine somatotropin (Sometribove) on ovarian function in lactating and nonlactating dairy cows. *J. Dairy Sci.* 76: 1002. 8. De la Sota R.L., C.A. Risco, F. Moreira, J.M. Burke and W.W. Thatcher. 1998. Efficacy of a timed insemination program in lactating dairy cows during summer heat stress. *Theriogenology* 49: 761. 9. DeLorenzo, M.A., T.H. Spreen, G.R. Bryan, D.K. Beede, and J.A.M. Van Arendonk.1992. Optimizing model: insemination, replacement, seasonal production and cash flow. *J. Dairy Sci.* 75:885. 10. DeLorenzo, M.A., and D.K. Beede. 1989. Using production and economic information for dairy management analysis. In Proc. International Stockmen's School. *Dairy Science Handbook* Vol. 19, p39. 11. Ferguson S.D. and D.T. Galligan. Reproductive programs in dairy herds. 1993. Proc. Central Veterinary Conference: 1: pp 161-178, Kansas City, MO. 12. Fogwell, R. 1998. Targeted breeding takes aim. http;//www.canr.msu.edu/dept/ns/ mdr119.html. 13. Folman Y., M. Kaim, Z. Herz, and M. Rosenberg. 1984. Reproductive management of dairy cattle based on synchronization of estrous cycles. *J. Dairy Sci.* 67: 153. 14. Folman, Y., M. Kaim, Z. Herz and M. Rosenberg. 1990. Comparison of methods for the synchronization of estrous cycles in dairy cows. 2. Effects of progesterone and parity on conception. *J. Dairy Sci.* 73: 2817. 15. Fonseca, F.A., J.H. Britt, B.T. McDaniel, J.C. Wilk, and A.H. Rakes. 1983. Reproductive traits of Holsteins and Jerseys. Effects of age, milk yield, and clinical abnormalities on involution of cervix and uterus, ovulation, estrous cycles, detection of estrus, conception rate, and days open. *J. Dairy Sci.* 66: 1128. 16. Gwazdauskas, F.C., W.W. Thatcher, C.A. Kiddy, M.J. Paape and C.J. Wilcox. 1981. Hormonal patterns during heat stress following $PGF_{2\alpha}$-Tham salt induced luteal regression in heifers. Theriogenology 16:221. 17. Heersche, G. and R.L. Nebel. 1994. Measuring efficiency and accuracy of detection of estrus. *J. Dairy Sci.* 77:2754. 18. Humblot, P. and M. Thibier. 1980. Progesterone monitoring of anestrous dairy cows and subsequent treatment with a Prostaglandin $F_{2\alpha}$ analog or Gonadotropin-Releasing Hormone. *Am. J. Vet. Res.* 41:1762. 19. Kelton, D.F., K.E. Leslie, W.G. Etherington, B.N. Bonnett, and J.S. Walton, 1991. Accuracy of rectal palpation and of rapid milk progesterone enzyme immunoassay for determining the presence of a functional corpus luteum in subestrous dairy cows. *Can. Vet. J.* 32: 286. 20. Kristula, M., Bartholomew, R. and D. Galligan. 1992. Effects of prostaglandin $F_{2\alpha}$ synchronization program in lactating dairy cattle. J. Dairy Sci. 75: 2713. 21. Larson, L.L. and P.J.H. Ball.1992. Regulation of estrous cycles in dairy cattle: A review. *Theriogenology*, 38:255. 22. Lucy, M., J.D. Savio, L. Badinga, R.L. de la Sota, and W.W. Thatcher. 1992. Factors the affect ovarian follicular dynamics in cattle. *J. Anim. Sci.* 70: 3615. 23. Lucy, M.C., J.S. Stevenson and E.P. Call. 1986. Controlling first service and calving interval by prostaglandin $F_{2\alpha}$, gonadotropin-releasing hormone, and timed insemination. *J. Dairy Sci.* 69: 2186. 24. Macmillan, K.L. and H.V. Henderson. 1984. Analyses of the variation in the interval from an injection of Prostaglandin $F_{2\alpha}$ to oestrus as a method of studying patterns of follicle development during dioestrus in dairy cows. *Anim. Reprod.* Sci. 6: 245. 25. Ott, R.S., K.N. Brestzlaff, and J.E. Hixon. 1986. Comparison of palpable corpora lutea with serum progesterone concentrations in cows. *J. Am. Vet. Med. Assoc.* 188: 1417. 26. Pankowski, J.W., D.M. Galton, H.N. Erb, C.L. Guard, and Y.T. Grohn. 1995. Use of prostaglandin $F_{2\alpha}$ as a postpartum reproductive management tool for lactating dairy cows. *J. Dairy Sci.* 78: 1477. 27. Pursley, J.R., M.O. Mee, M.D. Brown and M.C. Wiltbank. 1994. Synchronization of ovulation in dairy cows using GnRH and $PGF_{2\alpha}$. *J. Anim. Sci.* 72 (Suppl. 1):230 (Abstr.) 28. 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. 29. Pursley J.R., R.W. Silcox and M.C. Wiltbank. 1995. Conception rates at differing intervals between AI and ovulation. *J. Dairy Sci.* 78; 279 (Abstract). 30. Pursley J.R, M.O. Mee, and M.C. Wiltbank.1995. Synchronization of ovulation in dairy cows using $PGF_{2\alpha}$ and GnRH. Theriogenology 44:915. 31. Pursley, J.R., M.C. Wiltbank, J.S. Stevenson, J.S. Ottobre, H.A. Garverick and L.L. Anderson.1997. Pregnancy rates for artificial insemination at a synchronized ovulation of synchronized estrus. *J. Dairy Sci.* 80:295. 32. Putney, D.J., S. Mullins, W.W. Thatcher, M. Drost and T.S. Gross. 1989. Embryonic development in superovulated dairy cattle exposed to elevated ambient temperatures between the onset of estrus and insemination. *Anim. Reprod. Sci.* 19:37. 33. Risco, C.A., B.I. Smith, J.S. Velez and R. Barker. 1998. Management and economics of natural service bulls in dairy herds. *Comp. Cont. Edu.* In Press. 34. Risco, C.A., M. Drost, L.Archbald, F. Moreira, J. Burke and W.W. Thatcher. 1998. Timed artificial insemination in dairy cattle. *Comp. Cont. Edu.* In Press. 35. Roche, J.F. 1975. Control of the time of ovulation in heifers with progestational and gonadotropic-releasing hormone. *J. Reprod. Fertil.* 43:471. 36. Rodriguez, T.R., W.C. Burns, D.E. Franke, J.F. Hentges, W.W. Thatcher, A.C. Warnick, and M.J. Fields. 1975. Breeding at a predetermined time in the bovine following $PGF_{2\alpha}$ + GnRH. *J. Anim. Sci.* 40 :188 (Abstract). 37. Rosenberg, M., M. Kaim, Z. Herz and Y. Folman. 1990. Comparison of methods for the synchronization of estrous cycles in dairy cows. 1. Effects on plasma progesterone and manifestation of estrus. *J. Dairy Sci.* 73: 2807. 38. Savio, J.D., W.W. Thatcher, G.R.

Morris, K. Entwistle, M. Drost, and M.R. Mattiacci. 1993. Effects of induction of low plasma progesterone concentrations with a progsterone-releasing intravaginal device on follicular turnover and fertility in cattle. *J.Reprod. Fertil.* 98: 77. 39. Schmitt, E.J.P., T. Diaz, M.Drost and W.W. Thatcher. 1996. Use of a Gonadotropic-Releasing Hormone agonist or Human Chorionic Gonadotropin for timed insemination in cattle. *J. Anim. Sci.* 74:1084. 40. Silcox, R.W., F.L. Powell, J.R. Pursley and M.C. Wiltbank. 1995. Use of GnRH to synchronize ovulation in Holstein cows and heifers treated with GnRH and prostaglandin. *Theriogenology* 43:325. 41. Sirois, J. and J. Fortune. 1988. Ovarian follicular dynamics during the estrous cycle monitored by real time ultrasonography. *Biol. Reprod.* 39: 308. 42. Smith, M.W. and J.S. Stevenson. 1995. Fate of the dominant follicle, embryonal survival, and pregnancy rates in dairy cattle treated with prostaglandin $F_{2\alpha}$ and progestins in the absence or presence of a functional corpus luteum. *J. Anim. Sci.* 73: 3743. 43. Staples, C.R., W.W. Thatcher and J.H. Clark. 1990. Relationship between various cyclicity and energy states during the early postpartum period of high producing dairy cows. *J. Dairy Sci.* 73:938. 44. Stevenson, J., M.O. Mee and R.E. Stewarad. 1989. Conception rates and calving intervals after prostaglandin $F_{2\alpha}$ or prebreeding progesterone in dairy cows. *J. Dairy Sci.* 72: 208. 45. Stevenson, J.S., Y. Kobayashi, M.P. Shipka and K.C. Rauchholz.1996. Altering conception of dairy cattle by Gonadotropin-Releasing Hormone preceding luteolysis induced by prostaglandin $F_{2\alpha}$. *J. Dairy Sci.* 79:402. 46. Stevenson, J.S., M.C. Lucy and E.P. Call. 1987. Failure of timed inseminations and associated luteal function in dairy cattle after two injections of Prostaglandin $F_{2\alpha}$. *Theriogenology* 28:937. 47. Stott, A.W. and M.A. DeLorenzo. 1988. Factors affecting profitability of Jersey and Holstein Lactations. *J. Dairy Sci.* 71:2753. 48. Thatcher, W.W., K.L. Macmillan, P.J. Hansen and M. Drost 1989. Concepts for the regulation of corpus luteline function by the conceptus and ovarian follicles to improve fertility. *Theriogenology* 31:149. 49. Twagiramungu, H., L.A. Guilbault, and J. Dufour. 1995. Synchronization of ovarian follicular waves with a gonadotropin-releasing hormone agonist to increase the precision of estrus in cattle: a review. *J. Anim. Sci.* 73: 3141. 50. Van Cleeff, J.K., M. Drost, and W.W. Thatcher. 1991. Effects of postinsemination progesterone supplementation on fertility and subsequent estrous responses of dairy heifers. *Theriogenology* 36: 795. 51. Wolfenson, D., W.W. Thatcher, J.D. Savio, L. Badinga and M.C.Lucy. 1994. The effect of GnRH analogue on the dynamics of follicular development and synchronization of estrus in lactating dairy cows. *Theriogenology* 42:633.