OVSYNCH: A Method for Breeding Dairy Cows Without Doing Heat Detection

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Estrus detection rates are too low on many dairy farms using artificial insemination (AI). With perfect detection and no anestrus, all cows should be seen in estrus every 21 days and the average interval from the end of the postpartum waiting period (PPWP) to first AI would be the midpoint of one estrous cycle or about 10 days. However Minnesota DHIA heat detection rate was 43% for 1994, causing average time of first AI to be 30 to 35 days, rather than 10, after the PPWP. So average days in milk (DIM) at first AI in herds with a 60 day PPWP is usually 90 to 95 days rather than the theoretical possibility of 70 days.

Emphasis on 12 to 12.5 month calving intervals for dairy farm production efficiency has focused attention on the three factors which determine average DIM at first AI and at conception: 1) conception rate per breeding, 2) PPWP, and 3) estrous detection or AI submission rate. Minnesota 1994 DHIA conception rate was 52% so there is not much room for improvement here--as there appears to be a biologic cap on this parameter at about 50 to 60%. Some herds have reduced average days open by shortening their PPWP from 60 to 50 days or even less, but this causes some management difficulties due to the wide range in lactation lengths within a herd. **Therefore the most productive approach to improved dairy herd reproductive performance, especially average days open, is by working to increase heat detection or AI submission rates.** Greatest changes in average DIM at first AI can be made by using an estrous control program that allows appointment AI at a predetermined time after the PPWP. For example, average days to first AI from the end of the PPWP could be 3.5 if the program was repeated every week, 7 if repeated every 14 days, or 10.5 if repeated every 3 weeks.

The Ovsynch program, developed by dairy scientists Pursley, Wiltbank and others at the University of Wisconsin, is a new idea in bovine estrus control designed to allow AI without estrus detection in dairy cows (see Hoard's Dairyman: Aug 25 and Nov 10, 1995 and Mar 25, 1996; Dairy Herd Management: Jun 1995; and Theriogenology 1995, #44:915-923). This procedure has the effect of raising estrus detection rate (better named AI submission rate here) to 100% while hoping to maintain reasonable conception rates. Thus Ovsynch emphasizes pregnancy rate (the product of heat detection or AI submission rate X conception rate) as the way to improve overall herd reproductive efficiency. To further illustrate, note the calculations on the following table:

Reproductive Management System

	Conventional	Estrus Control & Appt AI	
1. Estrus detection or AI submission rate	43%*	100%	
2. Conception rate	52%*	35%	
3. Pregnancy rate 1 cycle (#1 X #2)	19%	35%	*1994

Minnesota DHIA averages.

It is apparent by this example that some sacrifice in conception rate in exchange for a 100% estrus detection or AI submission rate can be worthwhile when pregnancy rate is the endpoint.

In the Ovsynch program, each cow gets three injections for each breeding: first is GnRH on day 1, second is prostaglandin F2 alpha (PGF) on day 8, and third is another GnRH on day 10 with AI 18 to 24 hours later on day 11. [Note: Some of these time intervals are still being studied and could change in the future.]

Day 1	Day 8	Day 10	Day 11
	<-36-48 hrs>	<16-24 hrs->	
Inject GnRH	**Inject PGF**	**Inject GnRH**	**AI**

What is the purpose of each of these injections?

Injection #1

(GnRH = Cystorelin® or Factrel®) on day 1 "assures presence of a CL (needed to keep cows from coming into heat before the next injection on day 8 and to make them PGF responsive on day 8) and synchronizes growth of a new follicular wave".

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Injection #2

(PGF = Estrumate® or Lutalyse® on day 8 "to regress any CL's present and allow the new dominant follicle to proceed toward ovulation".

Injection #3

(GnRH = Cystorelin® or Factrel®) on day 10 "to cause the dominant follicle to ovulate". Users of this protocol must be aware that this second GnRH injection has the effect of cutting short full development of behavioral signs of estrus so AI should be based on appointment timing rather than on detection of estrus (ProcSocExpBiolMed 1976,#151:84 and JDairySci 1996,#79:402). Stevenson (Hoard's Mar 25, 1996:250) described a GnRH/PGF protocol without the second GnRH treatment where AI would be based on estrus detection.

What is the evidence that Ovsynch controls CL function and ovulation as needed for the method to work (when two injections of PGF 11 to 14 days apart are normally needed to get all cows in a group to have a synchronized estrus)?

1st Injection

From ultrasound observations after GnRH treatment, "18 of 20 lactating cows ovulated and formed a new or accessory CL and this injection initiated or was coincident with initiation of a new follicular wave in 20 of 20 lactating cows" (Therio 1995,#44:915).

2nd Injection

"Only 50% of a randomly cycling group of cows responded with estrus to one injection of PGF but 85% responded to one injection of PGF when it was preceded by GnRH [the GnRH agonist buserelin in this case] in 7 days" (JAnimSci 1992, #70:1904). However, in previous bovine reproduction research, a single injection of the GnRH product Cystorelin during diestrus was not able to prolong estrous cycle length (AmJVetRes 1977,#38:1153). Without this effect, it seems questionable that the ovarian status of most or all cows on Ovsynch will be such that one PGF injection could control estrus in most or all cows where all stages of the estrous cycle are potentially present at the time of first GnRH injection.

3rd Injection

The ability of the second GnRH injection to cause the dominant follicle to ovulate was also substantiated by ultrasound when 20 of 20 lactating cows ovulated between 24 and 32 hours after the second GnRH injection (Therio 1995,#44:915).

What pregnancy rates have been achieved?

The Sept. 10, 1995 Hoard's article reported Ovsynch versus control results for 333 cows on 3 Wisconsin dairy farms, with Ovsynch cows having "the same conception rate as control animals (about 40 percent) and 23 fewer days open (98 versus 121)"; with a net benefit of +$71 per cow per calving interval. In Therio 1995, #44:915, pregnancy rates of cows given PGF 48, 24 or 0 hrs prior to the second GnRH were 55%, 46% and 11% respectively, with 22 cows per group. The following table shows recently reported (Hoard's Dairyman Mar 25, 1996:250) pregnancy rates with Ovsynch, where various intervals between the second GnRH and the appointment AI were studied:

Time from Second GnRH to Appt AI	Number of Cows	Percent Pregnant
0	148	37%
8	147	40%
16	146	44%
24	146	40%
32	146	32%

To date, no other groups have published Ovsynch breeding results. We have bred a group of cows at the West Central Experiment Station dairy in Morris, Minnesota by this method (the AI day was July 13--the hottest day of the summer in Morris!!). Our pregnancy rate was 19% in 48 dairy cows treated and bred according to the plan, but 4 of another 6 Ovsynch cows became pregnant when bred 24 hours early, based on signs of estrus for an overall pregnancy rate of 13 (24%) out of 54. Another farm used Ovsynch in September 1995 on 24 cows, with a pregnancy rate of 25%.

Does Ovsynch work in heifers?

Ovsynch works better in lactating dairy cows than in heifers. In fact it is recommended that these methods be used only on lactating dairy cows and not on heifers. For some reason, heifers are less predictable in their response to these treatments than are lactating cows. In our Morris trial, 36 heifers were treated with Ovsynch (24 rather than 48 hours from PGF to 2nd GnRH) with a pregnancy rate of 28%.

How and when has pregnancy diagnosis been done in the Wisconsin trials?

Ultrasonography was used for pregnancy diagnosis in all the Wisconsin trials at 25 to 35 days after AI which raises at least two issues for consideration. First, this is 7 to 10 days earlier than the time at which pregnancy diagnosis by rectal palpation for a fetal membrane slip can be done. This difference in time after breeding when pregnancy, or more importantly the absence of pregnancy as the need to be retreated and rebred ASAP,

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is detected will affect the interval between repeat services in a system which completely eliminates AI based on estrus detection.

Thus veterinarians may feel increased pressure for earlier pregnancy diagnosis via current methods or to incorporate new methods such as ultrasound if they can be used earlier after breeding.

Secondly, it should be recognized that earlier post-breeding diagnosis of pregnancy is likely to show higher rates of early embryonic death (EED). Currently diagnosis from 35 to 60 days after breeding allows appreciation that about 5% of pregnancies diagnosed at this stage succumb to EED. Research on EED indicates pregnancy diagnosis at 25 to 35 days after breeding is likely to raise EED rate to about 10% (JAVMA 1978,#173:973 & 1979,#175:466). This does not mean that diagnosis of bovine pregnancy by ultrasonography is inherently more detrimental than palpation methods used later after breeding; rather it shows the effect of earlier diagnosis when the natural process of attrition is still underway.

Will Ovsynch work in anestrus cows?

Probably not. While GnRH was able to induce ovulation in most (9 of 10) cows at 14 days postpartum, (JAnSci 1974,#39:915), cows ready for rebreeding that are not cycling due to true ovarian inactivity have not responded to GnRH with improved reproductive performance over untreated controls with the same problem (AmJVetRes 1980,#41:1762 & JDairySci 1983,#66: 1721). Therefore cows with inactive ovaries after the PPWP are not likely to respond to the Ovsynch regime.

In our trial at Morris, a blood sample was taken at the time of PGF injection for progesterone assay and 15 (28%) of the 54 cows had little or no progesterone at that time, indicating they did not have a CL that would be able to respond to the PGF injection. Only 1 of those 14 cows became pregnant to timed Ovsynch breeding.

Can the GnRH products available in the USA (Cystorelin® and Factrel® equal the effects of buserelin?

Results reported above where a single GnRH injection 7 days before a single PGF injection increased estrus response rate from about 50% with one PGF treatment only to 85% are the basis for much of the Ovsynch theory of effectiveness, but the GnRH used in this trial was an analog named buserelin which is marketed as Receptal® (Hoechst) in much of the world but not in the USA. Buserelin is more potent and longer acting (JAnSci 1985,#61:224) than the two GnRH products currently available in the USA.

Are changes improvements in timing of the injections and/or AI are likely?

Time will tell but further research with this idea is likely because the ability to inseminate dairy cows without observation for standing estrus is very attractive, especially for dairy farmers in the Upper Midwest and Northeast USA using stanchion barn housing for their cattle.

Will the shift in emphasis from conception rate to pregnancy rate as the major indicator of dairy herd reproductive efficiency be generally understood and accepted?

Again, time will tell; but this is a change in mind set that dairy farmers need to make--especially our more conventional dairy farms in the Upper Midwest and Northeast.

Are there other estrus control methods for dairy cows?

Most veterinarians and dairy farmers have made use of the luteolytic activity of the PGF products to manage individual cows that have ovarian activity, i.e. especially presence of a mature corpus luteum (CL3), but are not seen in estrus. This use has expanded into several possible methods for using PGF products in routine reproductive management for the entire herd, but most of these methods are still based on observation for signs of estrus. It is possible to inseminate dairy cows following PGF treatment on an appointment basis. When appointment AI follows a single PGF injection--in cows known to have a CL3--better conception rates result when two inseminations (one on the third day and another on the fourth day after PGF injection) than from a single appointment insemination. However, the same comparison gives similar conception rates following two PGF injections 11 to 14 days apart.

What conception rates result from appointment AI following PGF by itself?

In the early days of PGF research, one trial in beef cows with calves and beef or dairy heifers (JAnSci 1974,#38:964) achieved a 56% conception rate with double appointment AI at 72 and 90 hours after a single PGF injection in females found to have a mature CL by rectal palpation, with 34 of 120 eliminated for lack of a CL after two examinations 7 days apart.

Dairy cows do not seem to respond to PGF as well as, or to be quite as fertile as beef cows with suckling

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calves and beef or dairy heifers. In dairy cows with unobserved estrus selected for PGF treatment by rectal palpation for a CL3, we reported a 59% conception rate in 76 cows bred at 72 and 96 hours after PGF (Therio 1978,#10:55). Eleven additional cows were assigned to this system but 2 were not inseminated, 6 were inseminated at one but not both of the assigned times and 3 were inseminated twice but not at the preassigned times; 3 of these cows became pregnant. Overall, a 56% pregnancy rate resulted in 87 unobserved estrus cows with a CL3 assigned to this protocol conceived as a direct result of the PGF treatment in a 5 day period. In the same trial, 78 similar cows with unobserved estrus and a CL3 were treated with PGF and assigned to be bred based on estrus detection. Within 5 days, 47 (60%) were seen in estrus and inseminated and 19 conceived for a 40% conception rate or a 24% pregnancy.

In a Minnesota dairy cow trial, 54 normal cows were given two IM injections of the PGF product cloprostenol (0.5 mg) 12 days apart with AI at 72 hours after the second injection, between days 55 and 61 postpartum. The conception rate to the appointment first AI was 35% versus 55% in contemporary herdmate controls, but average DIM at first AI were 58.5 for the appointment bred cows versus 81.2 for the controls. Average days open when all repeat services were based on heat detection were 88 for the appointment first AI group versus 104 for controls.

Summary

Ovsynch has been widely reported in the lay press and has understandably created considerable interest among dairy producers seeking better herd reproductive performance and/or elimination of heat detection. This program may produce acceptable results but, in my opinion, it is still too early to predict what results will be on your clients' farms. While many recent estrus control programs and heat detection aids are most helpful in freestall and loose housing arrangements, Ovsynch offers relief from the pressure to do 1x or 2x daily turn-out of cows for heat detection in herds housed in stanchion barns. Methods of estrus control (other than Ovsynch) using only PGF have produced similar results in dairy herd reproductive management trials but contemporary experimental comparisons are not yet available.

19027015 **PRODUCT**
NADA #141-063, Approved by FDA. **INFORMATION**

Nuflor®
(FLORFENICOL)

Injectable Solution 300 mg/mL

For Intramuscular Use in Cattle Only.
CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: NUFLOR is a solution of the synthetic antibiotic florfenicol. Each milliliter of sterile NUFLOR Injectable Solution contains 300 mg of florfenicol, 250 mg n-methyl-2-pyrrolidone, 150 mg propylene glycol, and polyethylene glycol q.s.

INDICATIONS: NUFLOR Injectable Solution is indicated for treatment of bovine respiratory disease (BRD), associated with *Pasteurella haemolytica, Pasteurella multocida,* and *Haemophilus somnus.*

RESIDUE WARNINGS: Animals intended for human consumption must not be slaughtered within 28 days of the last treatment. Do not use in female dairy cattle 20 months of age or older. Use of florfenicol in this class of cattle may cause milk residues. Do not use in veal calves, calves under one (1) month of age, or calves being fed an all-milk diet. Use in these classes of calves may cause violative tissue residues to remain beyond the withdrawal time.

WARNINGS: NOT FOR HUMAN USE. KEEP OUT OF REACH OF CHILDREN. This product contains materials that can be irritating to skin and eyes. Avoid direct contact with skin, eyes, and clothes. In case of accidental eye exposure, flush with water for 15 minutes. In case of accidental skin exposure, wash with soap and water. Remove contaminated clothing. Consult a physician if irritation persists. Accidental injection of this product may cause local irritation. Consult a physician immediately. The Material Safety Data Sheet (MSDS) contains more detailed occupational safety information.

For customer service, adverse effects reporting, and/or a copy of the MSDS, call 1-800-932-0473.

CAUTION: Not for use in cattle of breeding age. The effects of florfenicol on bovine reproductive performance, pregnancy, and lactation have not been determined. Intramuscular injection may result in local tissue reaction which persists beyond 28 days. This may result in trim loss of edible tissue at slaughter. Tissue reaction at injection sites other than the neck are likely to be more severe.

ADVERSE EFFECTS: Inappetence, decreased water consumption, or diarrhea may occur transiently following treatment.

DOSAGE AND ADMINISTRATION: NUFLOR Injectable Solution should be administered by **intramuscular** injection to cattle at a dose of 20 mg/kg body weight (3 mL/100 lbs). A second dose should be administered 48 hours later. Do not inject more than 10 mL at each site. **The injection should be given only in the neck musculature.**

NOTE: Intramuscular injection may result in local tissue reaction which persists beyond 28 days. This may result in trim loss of edible tissue at slaughter. Tissue reaction at injection sites other than the neck are likely to be more severe.

Clinical improvement should be evident in most treated subjects within 24 hours of the first injection. If a positive response is not noted within 24 hours of the second injection, the diagnosis should be re-evaluated.

STORAGE CONDITIONS: Store between 2°-30°C (36°-86°F). Refrigeration is not required. The solution is light yellow to straw colored. Color does not affect potency.

HOW SUPPLIED: NUFLOR Injectable Solution is packaged in 100 mL (NDC 0061-1116-04), 250 mL (NDC 0061-1116-05), and 500 mL (NDC 0061-1116-06) glass sterile multiple-dose vials.

REFERENCE: 1. Lobell RD, Varma KJ, et al. Pharmacokinetics of florfenicol following intravenous and intramuscular doses to cattle. *J Vet Pharmacol Therap.* 1994; 17:253-258.

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