EFFICACY OF LUTALYSE STERILE SOLUTION TO CONTROL ESTRUS IN BEEF CATTLE

J. W. Lauderdale, Ph.D.

Animal Health Research and Development
The Upjohn Company

Why Regulate Estrus?

Artificial insemination (AI) can give the herdsman the capability to use semen from progeny-tested sires. This selection capability can increase genetic gain resulting in greater cattle productivity of both meat and milk. In addition, control of veneral disease can be accomplished more easily by means of AI as compared to natural service. Even though AI has advantages, only about 50 to 60 percent of dairy cows are inseminated artificially for the United States, Canada and England. A smaller percent of beef cattle (less than 5 percent) and dairy heifers (about 20 percent or less) are inseminated artificially in the U.S.A.

The additional management time and skills needed for estrus detection have resulted in faulty estrus detection being the primary factor in the failure of herd managers to use AI to a greater degree in both dairy and beef cattle. The cost of estrus detection is justified only when AI results in pregnancy. Based on our current knowledge, estrus must be detected by man if either AI or hand mating programs are to be employed to breed cattle. In order to effectively use AI, dairy cattle must be observed at least twice daily for signs of estrus during most of the year and beef cattle must be observed at least twice daily during various intervals of time, usually at least 40 to 60 or 90 day intervals once each year.

The problem of estrus detection can be either (1) reduced if cattle can be inseminated and become pregnant during a three or four-day interval as compared to 20 to 24 days or (2) further reduced if cattle can be inseminated with reasonable probability of conception at a fixed time without estrus detection for at least one estrous cycle.

Management of Estrus with Lutalyse (PGF2α)

Early experiments in cattle revealed PGF2α to be luteolytic (yellow body regression) between days 5 to 18 of the estrous cycle with most animals in this range of their estrous cycles returning to estrus within 2 to 4 days after the administration of a sufficient dose of PGF2α. Cattle more than day 18 in their estrous cycle are not considered a problem because this population of cattle in a herd of PGF2α treated cattle would return to estrus and would be coincidentally fairly well synchronized with the cattle responding to PGF2α treatment. However, the nonresponding cattle which are less than day 5 in their estrous cycle are a major problem because their cycles would be from 15 to 20 days out of synchrony with the rest of the PGF2α treated animals. During the past 8 years, numerous synchronization of estrus management systems utilizing only PGF2α as the synchronizing agent have been studied. Most of these management systems have attempted

to manage the cattle from day 0 to 5 in their estrous cycles in a way to efficiently include them in a synchronized artificial insemination program. These management systems can be categorized in one of the following systems or as combinations or variations of one or more of these systems (Figure 1).

1. Two injections of PGF2α 11 days apart then breed after the second injection (a) according to detection of estrus (LLAIE) or (b) without reference to estrus at a present time of 75 to 80 hr (LLAI80).

2. Cattle are detected for estrus and inseminated for at least 4 days and on the morning of the 5th day all cattle not detected in estrus or previously inseminated are injected with a single injection of PGF2α. Breeding continues according to detection of estrus, i.e., a 9 to 10 day AI interval (AILAI).

3. Inject PGF2α then inseminate for 5 days according to detection of estrus; this system accepts that cattle in the first five days of their estrous cycle will not be synchronized (LAIE).

For each program, breeding at estrus subsequent to the first estrus can be with AI, bulls, or a combination of AI and bulls, depending on the goals of the breeding program (Figure 1).

The single injection program (LAIE) will be more effective relative to the number of injected cattle detected in heat within 5 days if either stage of the estrous cycle is known and cattle are injected on day 6 or later or if ovaries of cattle are palpated and a corpus luteum (CL) is present at time of injection. Effectiveness in the latter case will be dependent on the skill of the palpator to correctly identify a functional CL. Generally, the stage of the estrous cycle will be unknown for individual cows and palpation of ovaries will not be practical for most herds. However, the single injection program has utility in numerous reproductive management programs.

Many factors contribute to success of reproduction management; these factors are important also when time of breeding is to be regulated with Lutalyse. Some of these factors are:

1. Physical facilities must be adequate to allow cattle handling without being detrimental to the animal;

2. Nutritional status must be adequate prior to and during the breeding season. Nutrition has a direct effect on the age at initiation of estrus in heifers; on the postpartum interval to estrus following calving, and on conception;

3. Cattle must be ready to breed--they must be estrous cycling and must be healthy;

4. Estrus must be detected accurately if timed AI is not employed;

5. Semen of high fertility must be used;

6. Semen must be inseminated properly.

Lutalyse is effective only if cattle have a corpus luteum. Therefore, prepuberal and truly anestrous cattle will not respond to Lutalyse.

Definition of Measurements of Effectiveness

Estrus Synchronization = No. detected in estrus within 5 days after Lutalyse X 100 ÷ No. injected

Conception Rate = No. pregnant X 100 ÷ No. detected in estrus and A.I. This is a measurement of fertility.

Pregnancy Rate = No. pregnant X 100 ÷ No. injected. This is a measurement of reproductive performance and reflects estrus cycling percent and conception rate.

For example, if in a herd of 100 cows 60 were estrous cycling and were detected in estrus in one estrous cycle interval (24 days of AI), and if first service conception rate was 60 percent, then pregnancy rate would be 36 percent, i.e., 36 of 100 cows would be pregnant in 24 days in that natural mating or AI program. If the cattle were synchronized with Lutalyse, and if 60 of 100 cows were cycling before the start of the regular breeding season, then 60 cows would be detected in estrus within the first 5 days of AI and with a 60 percent first service conception rate 36 percent of the herd would be pregnant in 5 days. Lutalyse per se will neither increase the percent of the herd cycling nor alter conception rates. However, if large numbers of cattle are AI in a day or within a few hours by either an inexperienced or "out-of-condition" inseminator, conception rates can be decreased, sometimes severely.

Dose Selection

Various routes of administration (IM, SC, IV, IU, intravaginal) were reported to be effective in cattle so long as the proper dose was used for the specific route of administration. The intramuscular (IM) route has been selected for cattle since this route is practical and data demonstrated effectiveness.

In an attempt to identify an effective IM dose, about 1,215 beef cows and heifers in 18 herds were injected with 0, 5, 15, 25, or 35 mg PGF2α IM in the hip twice at an 11 (10 to 12) day interval. Cattle were assigned randomly in replicates within each herd in an attempt to equalize the distribution of cattle of similar age, weight, postpartum interval and semen source (bulls) among the dose groups. Cattle were inseminated (AI) at each estrus detected following the day of the second injection. Pregnancy examination was made between 60 and 100 days after the start of the breeding season. The breeding date for each pregnancy was confirmed by both non-return to estrus and by the palpator estimating stage of gestation and that estimate being similar to the recorded breeding date.

Based on percent cattle in estrus within 5 days, first service conception rate, and pregnancy rate within 5 days, the overall interpretation of these data led to the conclusion that 5 mi. Lutalyse (25 mg PGF2α) IM would provide consistently the best combination of return to estrus, conception rate and pregnancy rate of the doses studied.

Field Results

This presentation is based on data derived from a research program with commercial and purebred beef farms and ranches. Although this field research had several management factors imposed that would not ordinarily be factors in beef reproduction management, the data were generated under "real life situations" and I believe the data are predictive of what can be expected with commercial use of Lutalyse. This belief has been bourne out during the past two years of marketing Lutalyse--we have not encountered failures of Lutalyse efficacy that were not predicted from our field research.

In each of the investigations to be reported, cattle were assigned randomly in replicates of control and Lutalyse experimental groups. Attempts were made to balance age and semen source (bulls) between the experimental groups within herd so that no bias would be introduced in favor of either control or experimental groups. However, the presence of large numbers of Lutalyse-treated cattle in heat in a 5 day interval during the beginning of the breeding season stimulated an unusually increased percent of control cows to cycle early and become pregnant to AI at that estrus.

Double Injection Systems or LLAIE and LLAI80 (Figure 1)

About 3,800 beef cattle in about 50 herds were used to study, on a within herd contemporary comparison, the efficacy of the double injection program. Experimental groups of cattle were designated as either control or Lutalyse treated and either at estrus (LLAIE) or at 80 hours (LLAI80) for the first AI and at each subsequently detected estrus.

Cattle assigned to both LLAIE and LLAI80 were injected with Lutalyse intramuscularly in the hip twice at an 11 (10 to 12) day interval at a rate of 24 mg PGF2α per injection. Cattle of both control and LLAIE groups were observed for estrus and AI according to the normal procedures within herd at each detected estrus during the interval of the investigation.

Generally, cattle were observed for estrus twice daily and AI about 12 hours after the first observation of estrus.

Cattle of the LLAI80 group were AI at about 80 hours (usually between 75 and 80 hours) after the second injection of Lutalyse; under the experimental conditions of this study, LLAI80 cattle were

not rebred for at least five days after the 80-hour AI even if they were detected in estrus; cattle of the LLAI80 group were then AI at each subsequent estrus.

Dates of injections of Lutalyse were established such that the second injection would be administered the day prior to initiation of the normal breeding season within herd.

Significantly greater percentages of suckled cows and beef heifers were detected in estrus during days two to five of the AI season for LLAIE (47 percent cows, 66 percent heifers) compared to control groups (11 percent cows, 13 percent heifers).

Similar percentages of control (66 percent cows, 81 percent heifers) and LLAIE (70 percent cows, 84 percent heifers) cattle were detected in estrus at least once during the first 24 days (one estrus cycle) of the AI season. So, not all control cattle were exhibiting estrus even after the first 24 days of the breeding season.

First service conception rates were similar between control (about 60 percent) and LLAIE (about 60 percent) cattle for both days two to five and one to 24. These data reinforce previously reported data that conception rate was not altered following use of Lutalyse.

Pregnancy rate reflects both estrus synchronization and conception rate. During the synchronized interval, days two to five after second injection of Lutalyse, pregnancy rates were similar between LLAIE (36 percent) and LLAI80 (36 percent), but were greater for both of these groups when compared to controls (10 percent).

Pregnancy rates were similar among control, LLAIE and LLAI80 groups for days one to 18 (45 percent), days one to 24 (fifty percent) and days one to 28 (55 percent). Fourteen to 16 days of AI were required to achieve pregnancy rates in controls similar to a single timed AI.

The data presented in the preceding paragraphs are averages of all herds. Examples of the variety of results achieved among herds are presented in the following paragraphs.

In one herd, pregnancy rate was low (30 percent in 24 days) due to a conception rate problem. The records indicated 97 percent estrus detection for days two to five for Lutalyse-treated animals and 24 days for controls. But, low conception rates (30 percent first service conception rate) resulted in low pregnancy rates.

If conception rate in the herd is low, a high percentage of cattle won't be pregnant following use of Lutalyse.

In one herd of beef cows, pregnancy rate was similar among control and Lutalyse treated cows over each day of the first estrous cycle. The cows were beginning to estrous cycle at the start of the breeding season and did not synchronize to the Lutalyse injected 12 and one day prior to the breeding season.

Another beef herd, with 90 animals per treatment group, had something more than 50 percent pregnancy rate to timed AI and more than 85 percent of the herd pregnant by the 28th day of breeding. Obviously, the cattle were estrous cycling and conception rate was high. In two beef cow herds, pregnancy rate was more than 60 percent to timed AI and was more than 80 percent to 90 percent by day 28 of the breeding season.

These examples demonstrate that good results can be obtained if the cows are estrous cycling and conception rates are high.

We should recognize that with timed AI (LLAI80), unless all cattle are cycling, more services per conception (more semen) will be required per pregnancy since all cattle are AI at 75-80 hr whether or not they are cycling. Average services per pregnancy in the field study were 1.7 for controls, 1.8 for LLAIE and 2.5 for LLAI80.

The field results discussed above were based on about 4,000 cattle in about 50 herds. The results of that field investigation were reinforced by additional studies of LLAIE in about 1,800 cattle in about 24 herds of LLAI80 in about 1,600 cattle in about 11 herds.

Single Injection Systems

Single injection plus estrus observation or the LAIE system (Figure 1):

The LAIE cattle management system is IM injection of cattle with 25 mg PGF2α (5 ml Lutalyse) on the day before initiation of the breeding season followed by observation of cattle for estrus and breeding for 5 days. Breeding for the remainder of the breeding season is with AI, bulls or some combination of AI and bulls. If cattle ovaries are palpated accurately for the presence of a corpus luteum (CL) and only cattle with a CL are injected, the single injection would be expected to be similar in effectiveness to the double injection (LLAIE). In the absence of ovarian palpation, cattle of the LLAIE system compared to cattle of the LAIE system should have about a 20 percent to 25 percent greater first estrus detection rate and 20 percent to 25 percent greater pregnancy rate for breeding the first 5 days. The theoretical calculation is based on the data (1) that PGF2α is ineffective or less effective during days 1 to 4 or 5 after estrus as compared to days 6 to 18 after estrus and (2) that cattle usually have an 18 to 24 ($\bar{x}$ = 21) day estrous cycle; therefore, a single PGF2α injection per cow in a herd of randomly estrous cycling cattle should be about 75 percent to 80 percent as effective as the LLAIE system. These computed differences were confirmed in studies with 6 herds with about 1,400 beef cattle.

The field study of LAIE was completed in 17 herds with about 2,400 beef cattle.

The percent cattle detected in estrus the first time during days 1 through 5 was greater for LAIE vs control for both cows (57 percent vs 31 percent) and heifers (52 percent vs 28 percent). The percent cattle detected in estrus the first time during days 1 through 24 was similar between LAIE and controls for cows (76 percent vs 68 percent) and heifers (82 percent vs 82 percent).

The percentages of cattle detected in estrus during the first 24 days of AI were 68 and 82 for control cows and heifers and should be an over estimate of the percent of the herd having estrous cycles on the day of PGF2α injection.

Calculation of the predicted estrus detection rates would be as follows for single injections: 75 percent effective of 68 percent of estrous cycling cows equals 51 percent (actual was 57 percent in LAIE cows) and 75 percent effective of 82 percent of estrous cycling heifers equals 62 percent (actual was 52 percent for LAIE heifers). Thus the theoretical estrus detection rates and the actual estrus detection rates were similar, which reinforces the conclusion that a single injection of PGF2α yielded the predicted response.

First service conception rate would be expected to be similar between LAIE and control cattle. Conception rates for days 1 through 5 for LAIE and control cattle were 54 percent and 49 percent for cows and were 52 percent and 47 percent for heifers. Conception rates for days 1 through 24 for LAIE and control cattle were 63 percent and 53 percent for cows and were 57 percent and 53 percent for heifers.

Pregnancy rates for days 1 through 5 were greater for LAIE compared to control cows (30 percent vs 14 percent) and heifers (28 percent vs 12 percent). Pregnancy rates for days 1 through 24 were similar for LAIE and control cows (60 percent vs 56 percent and heifers (55 percent vs 49 percent). Pregnancy rates for days 1 through 28 tended to be greater for LAIE than control cows (66 percent vs 60 percent) and heifers (57 percent vs 52 percent).

These data on enhanced pregnancy rates after 5 days of AI with LAIE program are consistent with information published previously in three reports. The pregnancy rates for 5 days of breeding in the LAIE management system demonstrated that system to be effective.

Single injection on day 5 of breeding or the AILAI system (Figure 1):

The AILAI cattle management system is observation of cattle for estrus and AI for the first 4 days, inject cattle not detected in estrus with 25 mg PGF2α (5 ml Lutalyse) IM on the morning of day 5 and continue to observe cattle for estrus and AI accordingly on days 5 through 9 or 10, i.e., a 9 or 10 day AI season. Breeding for the remainder of the breeding season is with AI, bulls or some combination of AI and bulls (Figure 1).

This system takes into account that PGF2α is ineffective during the first 4 to 5 days after ovulation. The program does this through the four (4) day breeding program prior to Lutalyse injection. The four day duration is the minimum for effective control of the non-

responsive period after ovulation. Intervals of 5, 6 or 7 days are effective and are recommended by some AI companies. A second purpose of the 4 to 7 day pre-injection breeding interval is to allow for an assessment of estrous cycling in the herd. If all cattle are estrous cycling, about 4 to 5 percent of the herd should be detected in heat each day. If less than 3 percent of the herd is detected in heat per day (or a total of about 12 percent after 4 days of AI), then the cattle probably are not estrous cycling at a rate high enough to warrant use of Lutalyse at that time. Another option, if a low percent of the herd was detected in estrus, would be to have an accurate palpator identify those cattle that had a CL, but had not been bred, and inject only cattle with a CL with Lutalyse.

The AILAI program allows for about 17 more days postpartum to the time of Lutalyse injection, compared to the postpartum interval to the first injection of Lutalyse in the LLAIE or LLAI80 programs. This extra 17 days is very important in many beef cow herds to allow time for a greater percent of the herd to initiate estrous cycles following calving or to reach puberty.

This program also allows the inseminator to be re-educated in the art of AI during the first four days when only a relatively few cattle will be AI each day. During this interval the facilities will have minimal stress placed on them and if repairs need to be made, they can be made prior to the days after Lutalyse when relatively more cattle will be AI each day.

AILAI also appears to have great advantages for people just starting an AI program and for herds in which there is question about the percentage of the herd estrous cycling 10 to 12 days prior to initiation of the breeding season.

The percent cattle detected in estrus the first time during days 1 through 9 was greater for AILAI than for controls for cows (54 percent vs 38 percent) and heifers (64 percent vs 38 percent). First estrus detection rates for the first 24 days of breeding were similar between AILAI and control cattle for both cows (70 percent vs 73 percent) and heifers (77 percent vs 78 percent).

First service conception rates were concluded to be not different between cattle assigned to AILAI and control groups for days 1 through 9 (58 percent vs 64 percent for cows and 53 percent vs 56 percent for heifers) for days 1 through 24 (59 percent vs 63 percent for cows and 57 percent vs 59 percent for heifers).

Pregnancy rates were greater for AILAI than for control cattle for days 1 through 9 for cows (39 percent vs 26 percent) and heifers (45 percent vs 24 percent) and for days 1 through 24 for cows (56 percent vs 54 percent). Pregnancy rates for days 1 through 28 tended to be greater for AILAI than for control cows (63 percent vs 59 percent) and heifers (63 percent vs 59 percent).

The percentages of cattle detected in estrus the first time, first service conception rates and pregnancy rates should be similar between AILAI and control cattle for days 1 through 5 since the AILAI cattle would not have been injected with PGF2α. That was the case for beef heifers. In contrast, percent cows detected in estrus and pregnancy rate were each elevated for control cows for days 1 through 5. The basis for that difference is unknown since the cows were assigned randomly in replicates to the experimental groups, so these differences are assumed to be chance observations. However, this observation reinforces the conclusion that a 4 day estrus observation interval is not always as accurate a predictor of the percent of a herd cycling as we would like to have. Usually, if the estimate is incorrect, it is incorrect by overestimating the percent of the herd cycling.

The data on enhanced pregnancy rates after 9 days of AI with the AILAI management system are consistent with data published previously in five reports.

The greater pregnancy rate in the AILAI group for days 1 through 9 demonstrated the effectiveness of the use of PGF2α in that system of cattle management. The trend for more pregnancies in the AILAI group after 28 days of AI reinforces the conclusion that the AILAI management system was effective as measured by percent of herd pregnant. Since the cattle injected with Lutalyse that do not become pregnant to breeding at the first synchronized estrus (days 6 to 9 of the breeding season) would be expected to return to estrus during days 27 to 32, our data for 28 day pregnancy rate did not allow for the maximum difference between control and AILAI cattle. That the difference between control and AILAI cattle would be greater after 32 days of breeding is supported by data published by Dr. Ed Moody. In Dr. Moody's study with about 1,800 beef cattle, pregnancy rate after 32 days of AI was greater in cattle of the AILAI than control groups (72 percent vs 61 percent).

General Comments

A cattle estrus synchronization agent must be effective, have no harmful side, carryover or aftereffects, be simple to administer and relatively foolproof, and cost must be relative to benefits. The dose of Lutalyse recommended for cattle has been investigated extensively and no side effects of consequence have been detected with either the recommended dose or with doses of at least ten times greater. Intramuscular injections of Lutalyse are simple to administer and the expected cost relative to benefits appears to be acceptable.

Our overall conclusions are that Lutalyse offers a new approach to control of estrous cycles of cattle and that potential for timed insemination seems great.

Lutalyse isn't a cure-all. Cattle must be estrous cycling and have good fertility in order for Lutalyse to be an effective adjunct to reproduction management.

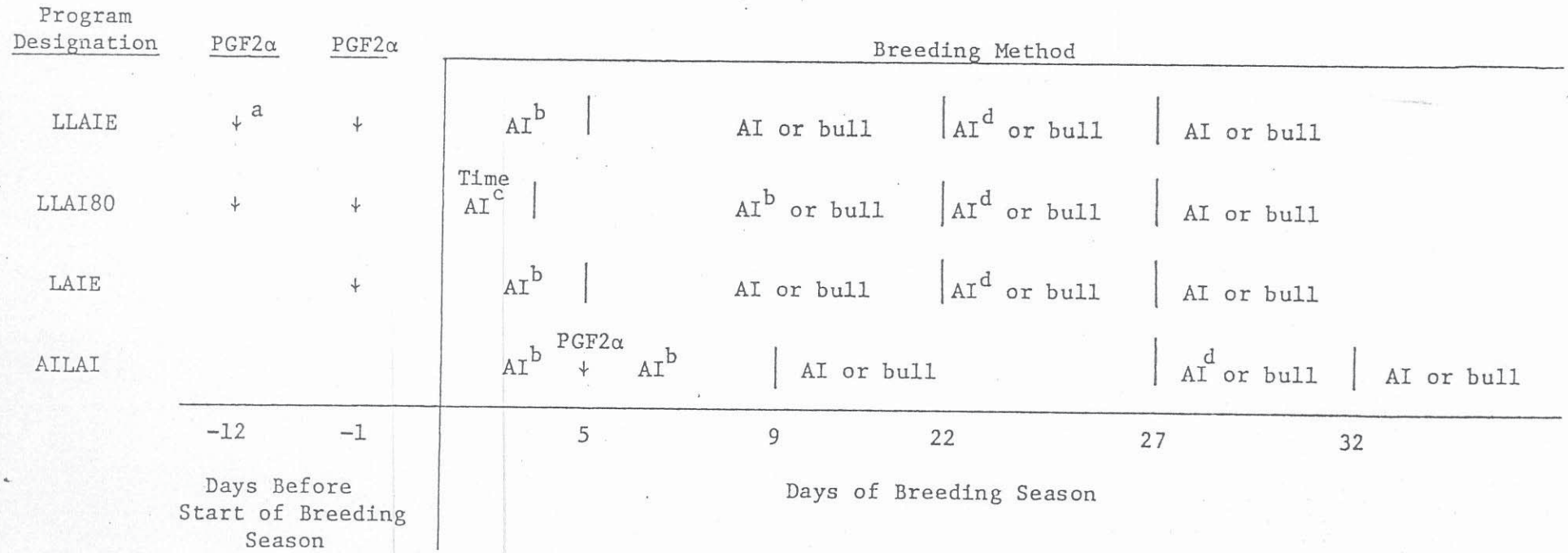
Under those types of conditions, Lutalyse would be expected to be extremely useful. The effectiveness of the LLAIE, LLAI80, LAIE and AILAI programs and various combinations of these programs supports the conclusion that Lutalyse should be useful in a variety of reproductive management situations with flexibility in AI programs.

Although extensive field investigations have not been completed on bull breeding of synchronized cattle, Dr. Ed Pexton, Colorado State University, has reported on the effective breeding of cattle with bulls at the synchronized estrus after Lutalyse. In a series of five studies with about 445 beef cattle, single sires were introduced to groups of about 20 females each for a 48 hour interval. Bulls were introduced 48 hours after the second of two lutalyse injections given 10 days apart. The conception rate (percent of cattle pregnant of those serviced) was 66 percent in the 48 hour breeding period. As always, females that were not estrous cycling did not come into heat and, therefore, were not serviced by the bull. In addition, the bull serviced about 76 percent of those females observed to be in heat. Thus, pregnancy rate of cattle observed in heat in 48 hours was about 50 percent. Pregnancy rate for all cattle was about 38 percent (75 percent in heat, serviced 76 percent of 75 percent; 66 percent conception rate), a value similar to that reported for either timed AI (LLAI80) or 5 days of AI (LLAIE).

A note of caution is in order about breeding synchronized cattle with bulls. Although cattle expressing estrus following Lutalyse are receptive to breeding by a bull, using bulls to breed large numbers of cattle in heat following Lutalyse will require proper management of bulls and females. Other than single sire mating with about 20 females per group in a small corral or hand-mating we do not, in my opinion, know how to effectively manage bull breeding of synchronized cattle.

And finally, a successful AI program can employ Lutalyse effectively, but a poor AI program will continue to be poor when Lutalyse is employed unless other management deficiencies are remedied first. An important factor in the success of use of Lutalyse is an understanding of what Lutalyse can and cannot accomplish. Expectations of success should be realistic relative to the cattle reproduction management each time Lutalyse is used.

Figure 1. Cattle Breeding Management with Lutalyse



a ↓ = 5 ml Lutalyse (25 mg PGF2α) intramuscular

b AI = inseminate upon detected estrus

c Timed AI at about 77 to 80 hr after the second injection of Lutalyse.

d Intervals during which cattle that did not become pregnant to AI during the first synchronized interval would be expected to return to estrus.