THE ECONOMIC VALUE OF CHANGES IN 21-DAY PREGNANCY RATE AND WHAT CONTROLS THIS VALUE

Victor E. Cabrera

University of Wisconsin-Madison, Department of Dairy Science

No single metric can describe comprehensively dairy cattle reproductive efficiency. A best approximation could be the 21-day pregnancy rate. Estimating the economic value of 21-day pregnancy rate is complex and difficult. One approach is to use Markov-chains as underline framework. Markov-chains can simulate the dairy herd dynamics of the interactions of reproduction, abortion, involuntary culling, mortality, and voluntary culling. Therefore, it is possible to find a herd structure matrix resulting from a defined 21-day pregnancy rate. The resulting herd structure indicates for example the herd's proportion of cows by parity, days after calving, and pregnancy status. Therefore, the value of a 21-day pregnancy rate can be estimated by the multiplication of the herd structure matrix by their net returns. Cow specific net returns can be estimated as the aggregation of milk income, feed costs, culling costs, mortality costs, new born value, and reproductive costs.

The marginal economic value of successive 21-day pregnancy rate 1% increments from 10 to 30% is depicted in Figure 1. These values represent a specific set of herd parameters and market conditions under constant reproductive costs. A marginally decreasing trend is noted. More economic value gains are expected for lower 21-d pregnancy rates. A total economic gain value of improving several percentage points can be estimated by accumulating individual 1% 21-day pregnancy rate increases. For example, improving 21-d pregnancy rate from 15 to 20% would represent an approximate economic gain value of $75.7/cow per year. This value is primarily controlled (in order) by: milk income over feed cost, new born value, reproductive cost, and culling and mortality costs.

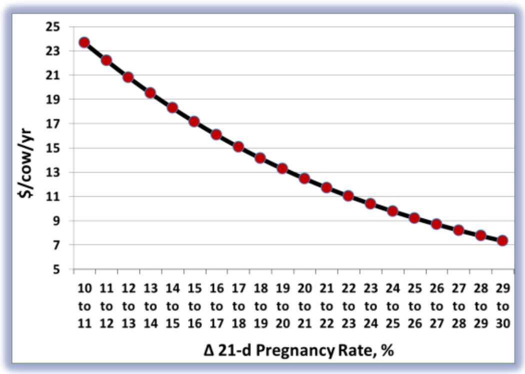

Figure 1. Marginal economic value of improving 21-d pregnancy rate

These economic gains may be under estimated. Improved reproductive efficiency (represented by greater 21-day pregnancy rates) would attain a greater farmer's ability for selective culling. Selective culling would have an impact on herd's milk production and productivity. Additional assessments among reproductive efficiency, selective culling, and herd's lactation curves are then warranted.

Victor E. Cabrera, Assistant Professor, Department of Dairy Science, University of Wisconsin-Madison, 1675 Observatory Dr., Madison, WI 53706, vcabrera@wisc.edu, 608-265-8506

THE ECONOMIC VALUE OF CHANGES IN 21-DAY PREGNANCY RATE AND WHAT CONTROLS THIS VALUE

Albert De Vries, University of Florida

Pregnancy rate (PR) is recognized as the primary measure of reproductive success for a group of dairy cattle. Pregnancy rates can be increased by increasing conception rates and/or 21-day service rates. The start and end of the eligible insemination period of individual animals also affects the group PR. Nationally, the average herd PR for cows is approximately 16%, but herd PR less than 10% or greater than 25% are observed. These PR indicate economic opportunity for improvement in dairy cattle reproduction. Improvements in reproduction typically translate in increased PR and increased profitability. Profitability is changed as a result of changes in herd demographics and the direct cost of the reproductive program.

Estimates of the economic value of an increase in PR vary widely. Most estimates in the literature were obtained by computer simulation. Differences are caused by varying assumptions in the biological model, for example shape of the lactation curves, prices and costs, management policy such as the eligible insemination period, and constraints such as a fixed total number of cows, milking cows, or milk quota. It is widely agreed that the economic value of a marginal increase in PR is greater at low levels of reproductive efficiency than at high levels, with a typical average marginal value of $25/cow/year which excludes the cost of the improvement. It appears that a reduction of replacement costs is the main component of the value of a marginal increase in PR. When the total number of cows is fixed, an increase in PR does not increase herd milk production much because the effect of the increased daily production of the lactating cows is reduced by the effect of fewer lactating cows and more dry cows. However, when the number of lactating cows is fixed, an increase in PR increases only the number of dry cows and hence the herd size, and results in a greater marginal value of PR. This principle also applies to herds that are affected by summer heat stress. The value of improvement in reproductive efficiency in the summer is much greater when the number of lactating cows is the constraint rather than when the total number of cows is the constraint.

It is further clear that some cows are more important to get pregnant than other cows, for example when they are still not pregnant in mid-lactation or have greater genetic merit. The availability of sexed semen, as well as reduced involuntary culling and greater reproductive efficiency also means that more heifer calves can be generated than are needed to replace culled cows. This creates options for dairy producers when they decide what type of semen (embryo) the cow should be impregnated with. Hence the economic value of changes in PR for these subgroups of cows may be very different from that of the whole herd. How these different economic values should affect efforts to get these cows pregnant is currently being investigated.

Albert De Vries, Associate Professor, Department of Animal Sciences, University of Florida,
L.E. "Red" Larson Dairy Science Building, Shealy Drive Bldg. 499 Rm. 104F, Gainesville, FL 32611-0910. P: (352) 392-5594 ext. 227, F: (352) 392-5595, http://www.animal.ufl.edu/devries, devries@ufl.edu

NEW ZEALAND PERSPECTIVE ON ANOVULAR COWS

Scott McDougall
Cognosco, Animal Health Centre, PO Box 21, Morrinsville, New Zealand

The dairy industry of New Zealand relies on gazing of pasture *in situ* as the primary form of nutrition. Breeding and calving are seasonal to align the period of maximum cow nutritional demands with maximal pasture growth. Breeding is undertaken following detection of estrus, with synchrony and fixed time insemination only used in those cows 'not detected in estrus' (NDE). Due to the requirement to commence breeding on a calendar date (rather than on some number of days after calving as used in non seasonal breeding systems) NDE cows are commonly examined 7 to 10 days before the start of the breeding program.

The herd level prevalence of cows NDE is about 20%, with 70-80% of cows have not ovulated (i.e. anovulatory anestrus (AA)), with the remainder having ovulated, but not expressed estrus (i.e. NDE but corpus luteum (CL) positive cows).

Cows that are defined as NDE are less likely to be bred, have lower conception rates, take longer to conceive and are more likely to fail to conceive during the breeding season than cycling cows. The cost of NDE is conservatively estimated to be >$NZ 20,000/annum for a 400 cow herd.

Risk factors for being NDE are multifactorial but include age, breed, peripartum disease, low body condition score at calving, 'late' calving relative to the start of breeding. The heritability of the interval from calving to first post partum ovulation is reported to be 0.18 to 0.30, which is higher than for other commonly measured reproductive traits.

Preventative strategies to reduce the prevalence of manage NDE or AA cows include management of prepartum nutrition to optimize BCS at calving, postpartum nutrition to increase the levels of non structural carbohydrates, reduction in milking frequency (e.g. from 2 x to 1 x daily) and physical separation of NDE/AA cows to increase foraging opportunities.

Not detected in estrus cows are commonly treated with gonadotropin releasing hormone (GnRH) and prostaglandin $F_{2\alpha}$ (PG) and GnRH at 5 then 2 day intervals ("Ovsynch"), respectively, with insertion of an intravaginal progesterone releasing device between the initial GnRH and PG. This treatment results in conception occurring 10-15 days earlier than where no treatment is provided, both in AA cows and in CL-positive NDE cows.

While the physiology and treatment of anovulation are relatively well understood, practical approaches to prevention, particularly via improving nutrition remain a challenge.

Contact details
Scott McDougall, Cognosco, Animal Health Centre, PO Box 21, Morrinsville, New Zealand
Ph +64 7 889 5159, fax: +64 7 889 3681, email: smcdoug@ahc.co.nz

Treatment of Anovular Dairy Cows

Jose Eduardo Santos
University of Florida, Dept of Animal Sciences, 1812 Shealy Dr PO BOX 110910, Gainesville, FL 32611-0920
PH: (352) 392-1958 ext. 251, FX: (352) 392-1931, EM: jepsantos@ufl.edu

Uterine Inflammation and Fertility

Klibs N. Galvão

Department of Large Animal Clinical Sciences, College of Veterinary Medicine

University of Florida – Gainesville, FL 32610.

Summary

The transition to lactation is a challenging period for a high producing dairy cow. This period is characterized by a decrease in dry-matter intake (DMI), leading to a sharp decrease in glucose and calcium, and an increase in body fat mobilization in the form of nonsterified fatty acids (NEFA), resulting in accumulation of products of incomplete oxidation of NEFA such as beta-hydroxybutyrate (BHBA). Neutrophils (PMN) are the main leukocyte type involved in bacterial clearance after uterine infection; however, during the period of negative energy balance, dairy cows experience a reduction in PMN function including reduced phagocytosis and killing capacity. This reduction is more pronounced in cows that develop uterine disease. Factors that account for such reduction are decreased PMN glycogen stores, decreased blood calcium concentration, and increased NEFA, and BHBA. Glycogen is the main source of energy for PMN phagocytosis and killing, calcium is an important second messenger for PMN activation, NEFA is associated with impaired PMN oxidative burst activity, and BHBA reduces PMN phagocytosis, and extracellular trap formation and killing of bacteria. If the immune system is not able to eliminate bacterial infection, disease is established. Early postpartum (< 21 DIM), cows are affected with metritis (severe and acute). Some cows clear the infection but other remain chronically infected (> 21 DIM) and the condition is termed endometritis. Regardless of the condition, the overall effect of uterine infection is damage to the endometrium and activation of inflammation with release of pro-inflammatory cytokines (TNFα, IL-1, and IL-6) and chemokines (IL-8). Damage to the endometrium is caused by the bacteria themselves and by release of proteolysis granules and reactive oxygen species by neutrophils. Pathogenic bacteria associated with metritis and endometritis are Escherichia coli, Arcanobacterium pyogenes, Fusobacterium necrophorum, and Prevotella maleninogenicus. E. coli releases the endotoxin lypopolisacharide (LPS) which affects GnRH and LH release, aromatase activity, and PGE to PGF ratio. The consequences of that are decreased estradiol production, decreased ovulation and extended luteal phase when ovulation occurs. A. pyogenes releases the cholesterol dependent cytotoxin pyolysin which damages the endometrium. Pro-inflammatory cytokines have also been shown to affect GnRH release, decreased endometrial oxytocin receptors, and to impair embryo development. The combined effect of bacterial infection and activation of inflammation is damage to the endometrium and embryo, delayed ovulation, extended luteal phase after ovulation, increased time to first insemination, decreased conception rates, increased time to conception, and increased pregnancy loss.

DIAGNOSIS AND TREATMENT OF UTERINE INFECTIONS

Stephen LeBlanc
University of Guelph

Nearly all dairy cows experience some bacterial contamination of the uterus after calving, and approximately one in three have some form of detectable infection and inflammation of the reproductive tract. The incidence of metritis is typically between 10 and 20 %, of clinical endometritis or purulent vaginal discharge (PVD) approximately 15%, and of subclinical or cytological endometritis a further 15%. These conditions increase the median time to pregnancy by several weeks. Cytological endometritis is diagnosed if there is > approximately 5% neutrophils in a sample of uterine cells obtained by brush or flush techniques. The diagnostic method is validated and fairly simple, but impractical for routine use in the field. There are a variety of validated and practical methods for diagnosis of PVD, and an intrauterine antibiotic therapy that mitigates the effect on reproductive performance. Recent results from a large clinical trial found that a common approach to treatment of endometritis, injection of prostaglandin, did not improve disease resolution or improve reproductive performance.

Worse postpartum negative energy balance is associated with more severe or prolonged uterine inflammation. Changes in feed intake and innate immune function precede both metritis and endometritis by several weeks. Infections with E. coli and A. pyogenes are associated with both metritis and PVD. There are new data to suggest that specific virulence factors in E. coli associated with adherence may be important in metritis and PVD. Cytological endometritis and PVD are overlapping but largely distinct conditions, and there are emerging data that cervicitis exists both concurrent with and separate from endometritis. Much remains to be learned about what initiates and sustains harmful inflammation of the reproductive tract, and such understanding is needed to inform development of effective treatments. Presently, commonly recommended best management practices for cows in the transition period are likely to be helpful to mitigate the risk of reproductive disease.

Stephen LeBlanc
Associate professor
Population Medicine, University of Guelph
Ontario, Canada
sleblanc@uoguelph.ca

Effects of Milk Production on Reproductive Physiology

Milo Wiltbank, Professor
University of Wisconsin-Madison, Department of Dairy Science, Madison, WI 53706
PH: (608)263-9413, FX: Fax (608)263-9412, EM: wiltbank@wisc.edu

LACK OF ASSOCIATION OF MILK PRODUCTION WITH REPRODUCTION

Stephen LeBlanc
University of Guelph

There is much debate about possible antagonism between high milk production and reproductive performance. The main question is whether fertility (the capacity for reproductive function and successful pregnancy) of dairy cows has in fact declined, as opposed to the success of management systems and people at meeting the metabolic, nutritional, housing, and social needs of increasingly productive animals but with no less inherent capacity to achieve and maintain pregnancy; and if fertility really has diminished, the extent to which this decline is caused by increased milk production. There is no doubt that production per cow has increased, but it is unclear how much of this increase can explain the apparent decrease in fertility. It is important to separate the biology of reproductive function from the effects of economically based management decisions about culling and continuation of breeding. Most traditionally-used measures of reproductive performance (calving interval, conception rate, non-return rate) are incomplete or severely biased outcome measures. Both herd and cow-level data should include as much information as possible on confounders of the relationship of production with reproduction. Population or herd-level data should not be used to make inferences about individual-level associations. Considering the quality of data and analytic methods in the published literature, it is not clear if there is any association between higher milk yield and the probability and timing of pregnancy, either among cows at various levels of production in a population at one time, or with increasing production over time.

We present results from a cross-sectional sample of data from approximately 100,000 cows in 3000 herds in Canada in 2005 that show that as herd annual production increased, herd pregnancy rate also increased. At the individual cow level, there was a neutral to slightly beneficial association of milk yield with time to pregnancy.

We submit that there is no inherent antagonism between milk production and reproductive performance, and that good nutrition, cow comfort, and attentive management provide the conditions for both high production and good reproductive performance.

Stephen LeBlanc
Associate professor
Population Medicine, University of Guelph
Ontario, Canada
sleblanc@uoguelph.ca

Genetic Selection as a Tool for Battling the Decline in Reproductive Performance in Lactating Dairy Cattle, by Kent A. Weigel, University of Wisconsin – Madison.

The decline in female fertility of lactating dairy cattle over the past forty years has been well-documented, especially within the Holstein breed. Many authors have claimed that a cause-and-effect relationship exists, such that selection for higher milk yield will inevitably lead to impaired fertility -- this 'defeatist' attitude frees some scientists from the burden of addressing the problem head-on. Research has shown a direct link between high milk production and some aspects of reproduction, such as ovulation rate and duration of estrus. However, other aspects of reproduction, such as anovulatory condition and embryonic loss, seem to be more closely associated with body condition score (and, hence, only indirectly related to milk yield). Moreover, the genetic correlation between milk yield and female fertility, albeit antagonistic, is moderate in magnitude (about 0.30). Therefore, it is possible to identify sire families that can provide both high milk production and satisfactory reproductive performance. Attempts to address the decline in female fertility through genetic selection began in 1994, with the introduction of genetic evaluations for length of productive life. Direct selection began in 2003, with the introduction of genetic evaluations for daughter pregnancy rate (measured as a function of days open), and additional traits such as cow and heifer conception rate were added in 2009. Early assessments of genetic trend indicate that selection for improved female fertility seems to be working, and although we may not return to the high conception rates seen several decades ago, it appears that we may be able to stop the decline. Recent research developments may be helpful as well. Our research indicates that selection for improved animal health, i.e. reduced susceptibility to common postpartum disorders such as ketosis, metritis/retained placenta, displaced abomasums, lameness, and mastitis, can be achieved using incidence data from on-farm herd management software programs. It has been well documented that improvements in early postpartum health are associated with enhanced reproductive performance. Lastly, the transition of dairy cattle breeding programs from traditional genetic evaluations based on progeny testing to early genomic evaluations based on DNA testing offers promise for improvement of fertility and other functional traits. Traits such as daughter pregnancy rate and length of productive life are difficult to improve through progeny testing, because daughter groups are generally not large enough to offset the heavy influence of environmental factors. Whole genome selection, on the other hand, is based on evaluation of associations between single nucleotide polymorphism (SNP) markers or haplotypes (i.e. blocks of SNPs inherited together due to close physical proximity on the chromosome) and the phenotypes of thousands of reference animals from the same breed. In this manner, accurate genetic evaluations for lowly heritable functional traits can be obtained early in life, and this can lead to more effective selection for female fertility and related traits.

Kent Weigel
Professor and Chair
University of Wisconsin
Department of Dairy Science
1675 Observatory Dr
Madison, WI 53706-1205
PH: (608) 263-4321
FX: (608) 263-9412
EM: kweigel@wisc.edu

USE OF GENOMICS TO IMPROVE FERTILITY

Peter J. Hansen, Dept. of Animal Sciences, University of Florida

Reproductive function is under genetic control but selection for the genes controlling reproduction has been difficult because of large environmental effects on reproduction and because easily-measurable traits that accurately describe fertility have not been identified. One possible approach to improve the rate of genetic progress is to select animals based on identification of markers for genes controlling reproduction. This approach, called genomic selection, can increase the rate of genetic progress because animals can be genotyped at an early age (even while embryos) and because the genetic merit of females can be estimated more accurately than previously.

As currently practiced, genomic selection depends on identifying mutations in the DNA called single nucleotide polymorphisms (SNPs). A single nucleotide mutation can cause the amino acid composition of a protein encoded by the gene to change, thereby altering its function, or can cause a change in how the gene is turned on or off in the cell, thereby affecting the amount of protein encoded by the gene that a cell makes.

The Bovine SNP50 chip that is now commercially available measures an animal's inheritance for 54,609 specific SNPs. Most of these SNPs are not in functional genes but many are close enough to functional genes that the genetic merit for some traits can be estimated with 70% reliability. Unfortunately, SNPs on the SNP50 chip do not accurately predict many reproductive traits including the most commonly used trait, daughter pregnancy rate.

Diagnostic tools with more SNPs have been developed, with one chip allowing genotyping for 800,000 SNPs. It is possible that these chips will allow for more accurate estimates of genetic merit for fertility. Another possible approach is to identify SNPs in the functional genes controlling reproduction. A few of these have been found and there are undoubtedly many more.

Genomic selection can reduce the cost of identifying genetically superior sires because bulls can be evaluated for genetic merit at an early age and in large numbers and a smaller number of bulls used for progeny testing. The impact on female selection is even greater. Without genomic selection, the accuracy of identifying genetically-superior females is low because of the lack of records on daughters. Moreover, almost all females must be retained in the herd to produce an adequate number of heifer replacements. For some traits (milk yield for example), genomic testing allows a reliable estimate of female genetic merit. When coupled with transvaginal oocyte recovery and in vitro fertilization, the selection intensity on the female side can be increased so that as little as 5% of the females produce all of the heifer replacements for a herd.

Given the potential impact of genomic selection on genetic progress for reproductive traits, more effort is needed to identify SNPs or groups of SNPs that predict reproductive potential.

Peter J. Hansen, Distinguished Professor and L.E. "Red" Larson Professor, Dept. of Animal Sciences, University of Florida, Gainesville FL 32611-0910. Ph: 352-392-5590 (office ext 243; lab ext. 238); Fax:352-392-5595; email: hansen@animal.ufl.edu; website: http://www.animal.ufl.edu/hansen

Producers Perspective on Importance of Health and Reproduction Traits

Don Bennink
North Florida Holsteins, 2740 W CR 232, Bell, Florida 32619
PH: (352) 463-7174, FX: (352) 463-1106, EM: gotmilk10@aol.com

Cover Slide: North Florida Holsteins sign and cow

Slide Number 1:
My slide number one is the same as previous speakers' slide number one. Even though the slide is the same, my message is different.

The dramatic difference in milk production is shown to be caused by the increasing milk level of the sires used on the population.

Slide Number 2:
Slide number 2 shows how this same population of bulls dragged down the fertility level of the females in the population.

The conclusion that is made is that breeding for production lowers fertility. In reality, this is as accurate as a prosecutor in a murder case saying the defendant killed the victim because he had a recently fired Colt 45 in his hand, yet the bullet that caused the death was a Winchester 30-30.

Since the beginning of time in our industry, it has been accepted that all other factors being the same, cows that are four to five months or more pregnant give less milk than their open counterparts. We bred for bulls whose daughters didn't breed back because bulls with daughters that didn't breed back gave more milk.

If you look far enough, you can always find something published that agrees with your opinion. I think the heritability for DPR is a lot more than 4 in well managed herds. Matthew Garcia came from a beef cattle ranch in New Mexico. He listened to one dairy researcher after another give presentations on the low heritability of fertility in dairy cattle. Yet on their beef cattle ranch, culling for fertility made a major difference in the number of calves they ended up with each year.

Slide Number 3 & 4:
Slides three and four show conclusions from his post doctoral research at Washington State University.

Slide Number 5:
Slide five shows that as of the April 2011 proof release the average AI bull is still negative for DPR.

Slide Number 6:
Slide 6 shows that of the proven bulls available with over a 75% Reliability for type, only 8 have a DPR of 3.0 or more.

Slide Number 7:
Slide 7 shows the 20 highest genomic bulls for Net Merit $ that semen is available. Note that some are negative DPR and only one is above 3.0. Denim is second highest NM $ and has a DPR of 3.5. For later reference – note that his dam is a Wizard daughter.

Slide Number 8:
We have been fanatics on breeding for DPR even before results came out to the public in 2003. Slide 8 shows a conception rate broken into quartiles by sire DPR. Note that the highest quartile has a conception rate nearly twice the lowest quartile in first calf heifers. Note that this number is 50% higher in second and greater lactation animals. I feel

that this is not because the lowest quartile became relatively more fertile, but because so many didn't breed back as first calf heifers resulting in their elimination from the equation.

Slide Number 9:
Slide number 9 is the result of one of the many studies that show that cows that maintain their body weight are more fertile. High fertility is closely correlated with genetic components of both fertility and the ability to maintain body weight.

Slide Number 10:
Slide 10 shows that fertility has the highest correlation with longevity of the major traits.

Slide Number 11:
This slide is our herd ranked by DPR. Note there are 38 at or above a 3.0 DPR. There are 3 at or above the unheard level of 4.0. This proves to us that we can improve fertility genetically. Remember – of all the proven bulls available in the industry only 8 are above 3.0.

Also note the effect of having Wizard as a maternal grandsire.

Slide Number 12:
This is the genomic ranking of our herd by NM$. Note that there is only one negative DPR on the list and that is a negative 0.1. This proves to us we can get fertility with all of the other economic traits if you really want to.

Slide Number 13:
Slide 13 is John Cole's demonstration of the ultimate level of NM$ that is theoretically possible. The highest genomic bull on the list was just over $900 vs. the 7515 shown here.

To demonstrate a principle, let's say the bars on the one-third on the left hand side of the page represent production; the third in the middle represent type and the third on the right represent health traits. Obviously, if we are to reach or approach John Cole's ultimate number, we have to be high in all three areas. Holsteins are strong in production and type, but weak in the health traits.

Typically, people are breeding the high NM$ or GTPI bulls to the high females. If neither have health traits, you aren't going to get there. You would never get good udders by breeding poor udder bulls to poor udder cows.

Prior to genomics, it was a huge guessing game as to exactly what were the strong and weak areas genetically. With breeding strong health and production to a strong health trait mate, the chances of getting all three were remote. Also, it was years before you knew because you had to wait for progeny tests to find out.

Now let's take Wizard. He is real strong in the health traits but weak on type and mediocre on production. Doing one on one with using Wizard daughters on high type and production bulls would take forever. Now we can do it by flushing, using genomics and sort out the one in ten that has high production, desirable type and strong health traits. The potential is substantial.

PERCEPTIONS OF PRECISION IN SIRE FERTILITY ESTIMATES: AN OBSTACLE TO GENETIC PROGRESS?

J. M. DeJarnette and R. L. Nebel
Select Sires, Inc.

Declining dairy cattle fertility over the past several decades has increased emphasis on sire fertility estimates in the selection process. Though sire fertility explains only a small portion of the variance in field fertility, sire selection is an easily implemented procedure as compared to more complex, labor intensive and often expensive changes to herd management. However, the precision of sire fertility estimates is often overestimated in the selection process. Irrespective of service numbers, environmental noise and binomial variation dictate that precision greater than ± 2 to 3% of the true value is unrealistic. Though subsequent fertility evaluations in time show a high degree of correlation, this is largely a reflection of a self-fulfilling prophecy as function of large numbers of common services in the rolling databases. Estimates based on independent data sources indicates sire fertility estimates explain 20 to 40% of the variation in sire fertility estimates in the contemporary data set depending on thresholds of accuracy (minimum numbers of services). These comparisons reconfirm that sire fertility estimates within ± 2 or 3% of the population average should be considered of normal fertility potential and fertility should have little to no influence in the sire selection process. In April 2011, the number of Holstein sires with Sire Conception Rate (SCR, USDA-AIPL) estimates ≤ -3 represented ~10% of all sires receiving evaluations but only 1.5% of the active AI population. In conclusion, sire fertility estimates are of tremendous value in providing feedback to the quality control programs of AI centers as they strive to provide a highly fertile, consistent quality product to their customers. Considering the known limitations in accuracy of sire fertility estimates as a function of environmental noise and binomial variation, the narrow range of distributions indicates an admirable accomplishment of these goals by most AI centers. Nonetheless, unwarranted emphasis on sire fertility in the selection process, to the extent of excluding sires with negative deviations from consideration, may unjustly handicap genetic progress of the herd (industry) for other economically important traits.

Raymond Nebel, V.P. Technical Service Programs, Select Sires, Inc., 11740 US Hwy 42 N # 143, Plain City, OH 43064-9494, PH: (614) 733-3494, FX: (614) 733-3494, EM: rnebel@selectsires.com

ISRAELI METHODS USED FOR OPTIMIZING DETECTION OF ESTRUS

Nadav Galon, Hachaklait Israel

Estrus detection in high producing dairy cows has been and remained a great challenge for farmers, veterinarians and scientists. All large farms in Israel today use automated electronic activity meters of various types and makes. On some farms automated technology is the sole mean of heat detection, while others still practice heat observation as well. Visual detection has been reduced in time and scale due to the automated technology and the rise in labor costs. In recent years there was a drop in heat detection rate and an increase in the rate of heifers and cows presented to the veterinarian for anestrus before being brought to the inseminator. The use of reproductive hormones is limited in Israel to undetected cows at the end of their voluntary waiting period, and mostly for treatment after ovarian palpation by the vet. Some cyclic cows are undetected due to sub-optimal operation of the available technology. Many cows post-calving suffer from metritis, negative energy balance and poor body condition. Market demand led farmers to shift production to summer, which is hot and humid. All of the above mentioned factors lead to reproductive difficulties and a grave impact on the economy of dairy farms.

Only a few controlled field studies compared between synchronization protocols and pedometry, and these did not show significant differences. It seems that with more on-farm technical support the present versions of activity meters could be used more effectively. Regular vet check-ups and consulting on farm can reduce the need for hormonal therapy. Periodic multi-farm data monitoring, updated benchmarks and goals, and retrospective farm data analysis may be used to provide a better understanding and management of the reproductive challenges in a specific farm.

Presently, and likely more so in the future, there is a growing consumer and regulatory awareness to the wide use of hormones in food producing animals. For years no new reproductive hormones have been released, while technology develops rapidly. In my understanding the future improvements in heat detection and reproduction lay in technology, not in hormones. The addition of new parameters to automated detection such as rumination, resting time, solid contents of the milk and various integrative algorithms, could be used to improve the performance of these systems. Reduced costs and easy regulation are key points. The scope of remote monitoring, less handling and interference in the welfare of cows may lead to improved reproductive management in the future.

Nadav Galon, Chief Veterinarian, Hachaklait Veterinary Services, P.O. Box 3039 Caesarea Ind. Park, Israel. Tel: +97246279610, e-mail: galon@hachaklait.co.il

ACTIVITY AS A TOOL TO INCREASE ESTRUS DETECTION RATES

Ray Nebel, Select Sires Inc.

Increased activity is long known to be an secondary indicator of estrus in cows. The benefit of measuring activity on the neck is that it's a non-invasive external measurement and gives the best cow comfort. The SelectDetect™ system collects activity data for each hour of the day and filters the data against the cow's normal activity and the activity of herd mates to accurately identify cows with "high activity" for the producer to identify as "to breed or not to breed". SelectDetect measures activity using an accelerometer. Accelerometers were developed first for the military, aerospace, and automotive industries. Accelerometers are now becoming more popular in industrial, medical and consumer devices, such as the iPads and iPods. Periodically, recorded data is downloaded wirelessly to the base station (~ 300 foot radius). The software running on the farm's computer downloads the activity data from the base station for analysis. Activity data either downloads to the base station by: "hardwire" or wirelessly by "blue-tooth" technology. Activity monitors have replaceable batteries with an expected life of approximately 18 months under normal power levels. To achieve the most accurate information possible from the SelectDetect system the activity data should be reviewed at least twice daily. If the cows and base station are within continuous range of each other it is recommended to review data prior to the desired breeding time. The farm manager must confirm high activity readings by entering either a heat, insemination, or do not bred event. This is necessary if evaluation of efficiency is desired. In a large field trial farm personnel inseminated cows at random intervals after the onset of high activity according to standard procedures, which in most herds was a once daily AI program. The hour activity exceeded the high activity threshold was used to determine interval from onset to AI. Conception rates from 4,126 services were recovered from 19 herds located in 8 states. The mean duration of high activity was 10.5 ± 0.1 h with a median of 10.0 h indicating a slightly skewed distribution. The distribution of duration of high activity was as follows: ≤4 h, 15.8%; 5 to 8 h, 17.2%; 9 to 16 h, 46.2% and ≥16 h, 21.3%. The parity by AI interval interaction significantly influenced conception rates. Among primiparous cows, a curvilinear relationship was apparent with optimum conception occurring at AI intervals of 13 to 16 hours after high activity and trended lower for both earlier and later AI intervals. Among multiparious cows, conception rates at intervals ≤12 h were different that those >16 h with 13 to 16 h being intermediate. Specifically, conception rates for primiparous and multiparious cows respectively were: 36 and 32.4% (0 to 4 h), 37.5 and 32.2% (5 to 8 h), 41.2 and 32.9% (9 to 12 h), 45 and 28.9% (13 to 16 h), and 37.7 to 23.3% (17 to 26 h). In conclusion, these results are consistent with similar studies based on observed mounting activity wherein optimum conception rates are obtained at AI intervals proximal to 12 hours after detected estrus (high activity) with shorter intervals appearing to be less compromising to conception rates that are longer intervals. The Select Detect system allows conception rates to be optimized because of 24–hour surveillance and precision of determining activity related to estrus.

R.L. Nebel, Select Sires Inc., 11740 US 42 North, Plain City, OH 43064-0143 email: rnebel@selectsires.com, Tel: 614-873-3732

STRATEGIES OF PRESYNCHRONIZATION BEFORE OVSYNCH

Jeffrey S. Stevenson
Kansas State University

Timed artificial insemination (TAI) programs became practical and popular in the late 1990's because they produced acceptable pregnancy rates per AI (PR/AI) and reduced the reliance on detection of estrus before submission of lactating dairy cows to AI. More than 85 to 90% of large (> 500 cows) dairy herds use timed AI programs because of their ease of administration in a management-labor system. This practicality is critical because while only 5.1% of all dairy herds in 2009 had more than 500 cows per herd, those herds produced more than 60% of the milk! First-service PR/AI in response to a TAI program runs in the mid-30% range.

Early studies indicated that PR/AI at first AI service after calving might be improved when cows were at specific stages of the estrous cycle before initiating a TAI program. Cows beginning the TAI program between days 5 and 13 of the estrous cycle had greater ovulatory responses and greater fertility than cows at other stages of the estrous cycle. Two early studies tested whether estrous cycles could be staged in cows to meet this ideal by applying two upfront injections of prostaglandin $F_{2\alpha}$ (named Presynch-12) administered 14 days apart and then initiating the TAI program 12 days after the second prostaglandin injection. Pregnancy rate per AI was greater in cows inseminated after the Presynch + TAI program than in cows submitted to the TAI program without presynchronization. Various permutations of the standard Presynch have been applied (e.g., Presynch-14, Presynch-11, and Presynch-10) where the two injections of prostaglandin were consistently administered 14 days apart, but the interval from the last injection to the onset of the TAI program was either 14, 11, or 10 days. In nearly all published studies, these Presynch systems have produced greater PR/AI in cows than in cows submitted to the TAI program without Presynch. Further, greater PR/AI were reported in cows treated with Presynch-11 than Presynch-14 before a TAI program, probably because more cows were at the ideal stage of the cycle after the Presynch-11 treatment.

Newer presynchronization systems have been tested (e.g., Double Ovsynch, PG-3-G, and G-6-G) in smaller numbers of cows but with promising results that seem to produce greater PR/AI than using only a TAI program without presynchronization. In some cases, Double Ovsynch and PG-3-G may produce greater PR/AI than the 2 standard Presynch variants (Presynch-11 or Presynch-10). These improved results may be realized in herds where more cows are anovulatory when submitted to the TAI programs before first AI services.

Because reproductive failure is often the leading cause of dairy cows leaving dairy farms (culling), reducing culling by increasing PR/AI increases the profitability for dairy producers and supports greater sustainability of dairy production. Maintaining a stable supply of milk for fluid and product consumption is essential to feed a growing world population.

Jeffrey S. Stevenson, PhD
Professor
Dept. of Animal Sciences and Industry
Kansas State University
Manhattan 66506-0201
tel: 785.532.1243
fax: 785.532.7059
email: jss@k-state.edu

STRATEGIES FOR PRESYNCHRONIZATION BEFORE RESYNCHRONIZATION

Paul M. Fricke, Ph.D.
Department of Dairy Science
University of Wisconsin - Madison

One strategy optimize fertility to Resynch and TAI has been to determine the optimal interval after TAI to initiate Resynch based on assumptions regarding the physiology of the estrous cycle (Fricke et al., 2003; Sterry et al., 2006). Assuming an estrous cycle duration of 21 to 23 d, initiation of Resynch 32 to 33 d after TAI should ensure that the first GnRH injection of Resynch occurs between Day 5 to 12 of the estrous cycle, a stage of the cycle when a CL should be present and that results in greater fertility when Ovsynch is initiated (Vasconcelos et al., 1999). Despite this logic, 16% to 22% of cows lack a CL 33 d after TAI (Fricke et al., 2003; Sterry et al., 2006). Based on this observation, an alternative approach might be to presynchronize cows before initiation of Resynch. Cows with a CL at the first GnRH injection of Resynch tended to have better fertility than cows lacking a CL (Fricke et al., 2003), and cows with high progesterone concentration at initiation of Resynch had greater fertility compared to cows with low progesterone (Silva et al., 2007). Administration of $PGF_{2\alpha}$ 34 d after TAI before initiation of a Resynch protocol 11 d later increased P/AI from 25% to 35% when compared to a Resynch protocol initiated 32 d after TAI but increased the interval between TAI from 42 to 56 d (Silva et al., 2007). Similarly, use of a Double-Ovsynch protocol for resynchronization increased P/AI from 30% to 39% when compared to a Resynch protocol initiated 32 d after TAI but increased the interval between TAI from 42 to 49 d (Giordano et al., 2009). New presynchronization strategies that improve fertility and decrease the interval between TAI are being developed. Presynchronization strategies before initiation of Resynch can improve fertility to Resynch TAI.

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SUPPLEMENTATION WITH PROGESTERONE IN TIMED AI PROGRAMS

Todd R. Bilby, Ph.D.
Texas A&M AgriLife Research and Extension

Many studies have evaluated the effects of supplemental intra-vaginal progesterone inserts within timed AI protocols in dairy cattle. The most common and recommended use of controlled internal drug release (CIDR; containing 1.38 g of progesterone) inserts within timed AI protocol is to insert the CIDR concomitant with the first GnRH injection, and, 5 or 7 d later, remove the CIDR insert concomitant with prostaglandin treatment.

The effects of CIDR insert treatment within timed AI protocols on pregnancy per AI (P/AI) are controversial. The inconsistent effects of treatment with CIDR inserts on P/AI could be attributed to differences in genetics, milk yield, type of timed AI protocols, percentage of anovular cows enrolled in the timed AI protocol, percentage of cows with properly synchronized estrous cycle following presynchronization protocols, and the progesterone concentrations resulting from CIDR treatment. It is well documented that the modern-day high producing dairy cow has elevated catabolism of steroids lowering the systemic concentrations of progesterone. A recent report illustrated that progesterone concentration still remained subluteal (< 1 ng/mL) when either a new or used CIDR were inserted into lactating high-producing Holstein dairy cows without a CL. Importantly, the low concentrations of progesterone resulting from CIDR treatment are sufficient to cause early resumption of cyclicity in anovular cows, to synchronize the estrous cycle by inhibiting ovulation of ovarian follicles, and, in cows without endogenous progesterone, to maintain the growth of dominant follicles until the insert is removed.

Recent studies conducted in multiple dairies demonstrated that CIDR insert treatment during timed AI protocols – for first AI and resynchronization – increased P/AI in 5 to 7% units. Although studies conducted in New Zealand had suggested that anovular cows would benefit from CIDR insert treatment more than cyclic cows, this has not been observed in studies conducted in USA dairy herds and conditions. A few studies conducted in the USA, however, have demonstrated that cows that did not have a corpus luteum (CL) at the start of timed AI protocols and were treated with a CIDR insert had greater P/AI than cows without a CL and not treated with a CIDR insert. Therefore, it is likely that CIDR treatment increases P/AI by improving synchrony of the estrous cycle of cows submitted to timed AI protocols, particularly those that start the timed AI protocols at inappropriate intervals of the estrous cycle (e.g. proestrus, estrus, and metestrus). The CIDR insert would prevent the cows from displaying estrus and ovulating during treatment even if a CL is absent because the low progesterone concentrations resulting from CIDR treatment inhibit LH pulsatile release and LH surge, preventing follicles from reaching ovulatory size and ovulating. Consequently, after CIDR removal, estrus and ovulation are tightly synchronized which is likely to improve P/AI after fixed time AI. Therefore, for cows being resynchronized the use of CIDR inserts may be particularly beneficial since a large percentage of cows start the resynchronization protocol at inappropriate stages of the estrous cycle regardless of interval from previous AI.

In conclusion, treatment with CIDR inserts results in faster resumption of cyclicity in anovular cows and heifers, tighter return to estrus in non-pregnant cows, and improved synchronization of the estrous cycle of cows submitted to timed AI protocols.

Todd R. Bilby, Associate Professor and Extension Dairy Specialist, Texas A&M System, Address: 1229 North U.S. Hwy. 281, Stephenville, TX, 76401; Tel: 254-968-4144, fax: 254-965-3759, email: trbilby@ag.tamu.edu

ECONOMIC COMPARISON: TIMED AI VS. NATURAL SERVICE

Natural service bulls (NS) remain to be used on many dairy farms, either for all inseminations or as “clean up” for animals that failed to get pregnant earlier. A widely used alternative system is timed artificial insemination (TAI). Economic comparisons between NS and TAI are scarce. A California study found a $10/cow/year advantage for TAI supplemented with estrus detection, compared to NS, assuming that the pregnancy rates (PR) of both systems were the same. A direct comparison of TAI without estrus detection and NS on a Florida farm, using a randomized study design, showed similar PR of approximately 25%. The direct cost of the NS bulls was greater than for the TAI system, however, mostly due to the cost of feeding the bulls. After accounting for the small differences in PR, the advantage of the TAI system was also $10/cow/year. Increased AI semen cost and a lower value of genetic progress of AI semen easily created an advantage of the NS system. Realistic greater feed cost for bulls, on the other hand, made TAI more advantageous. The opportunity of replacing NS bulls with additional cows in the same pen would further create an advantage of the TAI system. Differences in PR between both systems would quickly overwhelm the effect of differences in direct costs on profitability. It is possible that the good randomized study design results, obtained by careful researchers, may not be repeated in practice when compliance of protocols may be lower. A major question for individual farms is therefore what the PR of each system would be.

Albert De Vries, Associate Professor, Department of Animal Sciences, University of Florida,
L.E. "Red" Larson Dairy Science Building, Shealy Drive Bldg. 499 Rm. 104F, Gainesville, FL 32611-0910. P: (352) 392-5594 ext. 227, F: (352) 392-5595, http://www.animal.ufl.edu/devries, devries@ufl.edu

TIMED AI WITH OR WITHOUT ESTROUS DETECTION

Victor E. Cabrera

University of Wisconsin-Madison, Department of Dairy Science

The economic net present value of timed AI synchronization to ovulation programs could increase, remain, or decrease when estrous detection is included. The most important factor is the ratio between the conception rates of timed AI and estrous detection programs.

Let's demonstrate these facts with an example of two pure timed AI and a pure estrous detection reproduction programs defined in Figure 1. Double-Ovsynch is used for first service in both timed AI programs at 82 days after calving with a 45% conception rate. One of the timed AI programs continues with Double-Ovsynch resyncrhonizations every 49 days with a 39% conception rate (top curve). The other timed AI program continues with day 32 (D32) Ovsynch resynchronizations every 42 days (middle curve). The estrous detection program has a voluntary waiting period of 50 days after calving, a continuos estrous detection rate of 50%, and a conception rate of 30% (bottom curve).

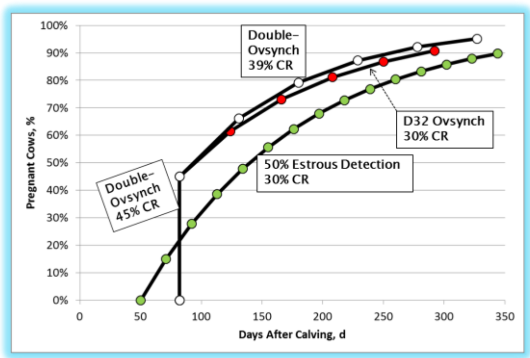

Figure 1. Survival curves of two timed AI programs and one estrous detection program

When the 50% estrous detection is included before and in between the Double-Ovsynch + D32 Ovsynch timed AI program, the net present value increases by $2.64/cow per year for the 30% estrous breeding conception rate and would change between -$15 and $21/cow per year for estrous detection conception rates between 27 and 33%, respectively (Figure 2).

When the 50% estrous detection is included before and in between the Double-Ovsynh + Double Ovsynch timed AI program, the net present value decreases by $22/cow per year for the 30% estrous breeding conception rate and would change between -$22 and $8/cow per year for estrous detection conception rates between 30 and 36%%, respectively (Figure 2). The net present value of including estrous detection before and in between the Double-Ovsynch + Double Ovsynch program would be greater than the pure timed AI program only if the estrous detection conception rate is 35% or greater.

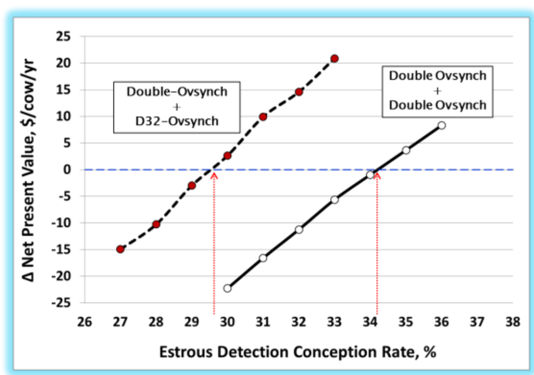

Figure 2. Economic value of including 50% estrous detection before and after timed AI programs

Victor E. Cabrera, Assistant Professor, Department of Dairy Science, University of Wisconsin-Madison, 1675 Observatory Dr., Madison, WI 53706, vcabrera@wisc.edu, 608-265-8506

EFFECTS OF LACTATION ON FERTILIZATION AND EMBRYONIC DEVELOPMENT IN LACTATING DAIRY COWS.

Roberto Sartori

Department of Animal Science, ESALQ, University of São Paulo (USP), Piracicaba, SP, Brazil 13418-900.

robertosartori@usp.br

During the last 50 years, the fertility in high-producing, lactating dairy cattle has decreased as milk production increased. Recent data show conception rates to first service to be around 32% in lactating cows, while in heifers it has remained above 50%. Fertilization does not seem to be the principal factor responsible for the low fertility in single-ovulating cows, since it has remained above 80%, except for heat stressed cows or cows bred inappropriately. On the other hand, early embryonic development is impaired in high-producing dairy cows, as observed by most embryonic losses occurring during the first week after fertilization. Milk production, body condition score, type and quantity of feed intake, and heat stress are all potential factors altering embryo quality. Among these multifactorial causes of the low fertility in lactating dairy cows, high feed intake associated with low circulating steroids concentrations may contribute substantially to reduced embryo quality. In order to minimize these problems, reproductive management programs that rely on the use of exogenous hormones for controlling the time of ovulation, or the strategic use of embryo transfer, may be necessary.

Maternal Regulation of Embryonic Development

Pat Lonergan
University College Dublin

Poor reproductive efficiency is a worldwide problem affecting the dairy industry. There is substantial evidence for an association between high milk production and the lower conception rate observed in cows compared to heifers. However, whether the decline in fertility is due directly to the level of milk production or other factors associated with lactation is unclear. There are various checkpoints along the developmental axis which could, in part, contribute to reduced fertility including suboptimal follicle development associated with poor oestrus exhibition, suboptimal oocyte quality, altered sperm transport and fertilization and/or a suboptimal reproductive tract environment incapable of supporting normal embryo development. The challenge is deciphering where the major problems lie. The major portion of embryo loss occurs very early during pregnancy, around or prior to maternal recognition of pregnancy at approximately Day 16, highlighting the importance of optimal embryo development in the days leading up to this critical period. A considerable proportion of embryo loss may be attributable to inadequate circulating progesterone concentrations and the subsequent downstream consequences on endometrial gene expression and histotroph secretion into the uterine lumen. Conceptus growth and development require the action of progesterone on the uterus to regulate endometrial function including conceptus–maternal interactions, pregnancy recognition and uterine receptivity for implantation. Experiments on the effects of progesterone on endometrial function and conceptus growth will be discussed.

Pat Lonergan, University College Dublin, Room 245, Vet Sciences, BELFIELD, IRELAND
PH: 353-1-6012147, FX: 353-1-6288421, EM: pat.lonergan@ucd.ie

Epidemiology of Pregnancy Loss in Dairy Cattle

Jose Eduardo Santos
University of Florida, Dept of Animal Sciences, 1812 Shealy Dr PO BOX 110910, Gainesville, FL 32611-0920
PH: (352) 392-1958 ext. 251, FX: (352) 392-1931, EM: jepsantos@ufl.edu

TECHNOLOGIES FOR EARLY PREGNANCY DIAGNOSIS

Matthew Lucy
University of Missouri

Pregnancy testing in dairy cattle has evolved over time. The simplest and perhaps the most definitive test for pregnancy is to wait until the cow gives birth to the calf. This approach is of little use in modern dairy practice because identifying the pregnant or nonpregnant (open) cows takes too long. The desire for an earlier pregnancy diagnosis led to the routine use of rectal palpation of the uterine contents for the purpose of detecting the pregnancy. Pregnancy diagnosis by rectal palpation has been pushed to its limit of detection (30 to 35 days after insemination) in an effort to identify open cows sooner after insemination. The need for additional sensitivity led to the introduction of transrectal ultrasound for pregnancy detection. Transrectal ultrasound can be used as early as 25 days after insemination but is more typically applied after day 30. There will always be the desire to perform pregnancy exams sooner after insemination so that the interval between first and second insemination can be reduced. Decreasing the interval between first and second insemination improves reproductive efficiency but if $PGF_{2\alpha}$ or timed AI are used then an accurate pregnancy diagnosis must be made before the program is applied. The earliest diagnoses (for example 25 days after AI) require the greatest skill and the most-specialized equipment (ultrasound). The situation has created an opportunity for the application of chemical pregnancy testing (for example, blood tests for pregnancy). Indeed, a recent report in *Hoard's Dairyman* cited rapid growth in the application of one blood test for pregnancy. If cattle were people then the solution would be simple. The human pregnancy produces copious amount of a hormone called hCG (human chorionic gonadotropin) that passes into the urine and can be detected by a simple lateral flow ELISA test. Unfortunately cows do not make a pregnancy-specific molecule that is detectable in the urine. There are, however, a series of candidate molecules associated with pregnancy in cattle. These molecules include (in order of detection): "early pregnancy factor", interferon-stimulated genes (ISGs), progesterone, and pregnancy-associated glycoproteins (PAGs). The "early pregnancy factor" is a promising candidate but its existence should be examined further because the available data are weak. Blood tests for PAG are seeing widespread commercial application. These tests may enable pregnancy detection as early as 25 days after insemination. There is also the future possibility of ISG tests that could determine pregnancy by 18 to 20 days after insemination. Both of the PAG and ISG tests have the capacity to significantly improve reproductive efficiency if applied on-farm. If in-line milk progesterone monitoring becomes a reality then pregnancy diagnosis will be done in real-time based on milk progesterone concentrations. An entirely new approach to managing reproduction will need to be developed that is based on the progesterone profile of the cow.

Dr. Matt Lucy, Professor of Animal Sciences, 158 Animal Sciences Research Center, University of Missouri, Columbia, MO 65211, Phone: 573-882-9897, Email: lucym@missouri.edu

OPTIMIZATION OF NONPREGNANCY DIAGNOSES FOR REPRODUCTIVE MANAGEMENT

Paul M. Fricke, Ph.D.
Department of Dairy Science
University of Wisconsin - Madison

Early identification of nonpregnant dairy cows post breeding can improve reproductive efficiency and pregnancy rate by decreasing the interval between AI services and increasing AI service rate. Thus, new technologies to identify nonpregnant dairy cows early after artificial insemination (AI) may play a key role in systematic management strategies to improve reproductive efficiency and profitability on commercial dairy farms. Transrectal palpation is the oldest and most widely used method for early nonpregnancy diagnosis in dairy cattle; however, a newer technology may someday replace transrectal palpation as the method of choice for nonpregnancy diagnosis in the dairy industry. Two events must transpire before this transition occurs. First, a technology must be developed that exceeds transrectal palpation in one or more of the attributes of the ideal early nonpregnancy test. Second and no less important, this new technology must be practically integrated into a systematic on-farm reproductive management strategy and empirically demonstrated to exceed the status quo of the industry in reproductive performance. Results from several recent studies indicate that positive pregnancy outcomes diagnosed by transrectal ultrasonography conducted 26 or 27 d after timed AI may be inflated due to pregnancy loss and/or diagnostic errors compared to pregnancy outcomes conducted 32 to 39 d after timed AI. Furthermore, fertility to timed AI after resychronization of ovulation was greater when initiated 33 d after timed AI compared to 19 or 26 d after timed AI. Taken together, these results support the counterintuitive notion that delaying pregnancy diagnosis may improve reproductive efficiency when combining ultrasonography with a hormonal protocol for timed AI to program nonpregnant cows for rebreeding due to the high rate of pregnancy loss and errors occurring too early post TAI.

Paul Fricke, Professor of Dairy Science, University of Wisconsin, Department of Dairy Science, 1675 Observatory Dr Madison, WI 53706-1205, PH: (608) 263-4596, FX: (608) 263-9412, EM: pmfricke@wisc.edu

Impact of transition cow nutrition and management on postpartum energy metabolism and health

Thomas R. Overton[1]
Department of Animal Science
Cornell University

The desired outcomes of successful transition management programs include a balance between high milk yield, maintenance of body condition score, incidence of health disorders related to metabolism and immunocompetence, and return to estrous and first service conception. Although many would suggest that decreased reproductive function is a consequence of high milk yield, recent information suggests that early lactation milk yield has poor relationships with return to estrous, first service conception rate, and calculated energy balance, and that feed intake during the transition period and early lactation along with the extent of mobilization of body condition have much stronger relationships with energy balance and reproductive function than milk yield.

The metabolic regulation and coordination of tissue function to support the biological changes occurring during late pregnancy and early lactation is extensive and exquisite, and involves many tissues including liver, muscle, and adipose tissue along with a number of other tissues. Normal adaptation to lactation includes some degree of insulin resistance to spare glucose oxidation in muscle and to facilitate adipose tissue mobilization; however, excessive insulin resistance – particularly in adipose tissue – appears to result in accentuated dynamics of DMI, NEFA, and BCS loss in the immediate peripartal period that likely predisposes cows to both increased health disorders and poorer reproduction along with potentially decreased milk yield. The most likely candidates for this phenomenon include overconditioned dry cows and cows with excessive energy intakes during the precalving period (either far-off or close-up). This has led to dry period nutritional strategies designed to control energy intake to meet, but not dramatically exceed, requirements during the dry period.

We believe that blood metabolites (NEFA and ketones) that have been most commonly associated with and used in troubleshooting of transition cow health issues have opportunity to be used to monitor opportunities in overall peripartal energy metabolism relative to reproduction and milk yield. In a large field study dataset, cows with elevated NEFA precalving and elevated NEFA and/or ketones postcalving were 15 to 20% less likely to become pregnant within 70 d post voluntary wait period than cows with lower concentrations of these metabolites.

In summary, the transition management challenge is to put systems into place (nutritional strategies, facilities, grouping management) that decrease individual variability in energy metabolism or that help to manage the inherent animal to animal variation that exists in our dairy production systems.

[1] Contact at 272 Morrison Hall, Ithaca, NY 14853. Phone (607) 255-2878; FAX (607) 255-1335; Email tro2@cornell.edu

Effects of Nutrition in the Transition Period on Reproduction

Elliot Block

While we can all agree that prepartum nutrition impacts health and reproduction of the postpartum dairy cow there is very little published work on the subject specifically related to reproductive outcomes.

Successful reproduction is a coordinated series of events that is on ongoing process from the birth of a heifer through maturity. While short term nutritional factors certainly influence the odds of a successful pregnancy, the process has to be viewed as metabolic regulation. Therefore, reproductive failure should be considered a metabolic disease not unlike the currently accepted metabolic diseases that occur in the early postpartum period (hypocalcaemia, ketosis, fatty livers, displacements, etc.). In this regard, when we are better able to understand more of the relationships between metabolism and reproductive outcomes we can model the processes and find better or more precise interventions to improve the odds of success. If we accept reproductive failure as a metabolic disease then we know that no one factor can be isolated as having a large impact on reproductive success in all situations.

As far as individual factors and their relation to reproduction there is information available on protein nutrition, time fed a transition diet, and fatty acid nutrition separate from energy nutrition (energy nutrition will be discussed in another conference at this meeting). Metabolizable protein (MP) nutrition in the transition diet appears to affect reproduction (and production) positively. Many transition diets formulated for 800 to 1000g/d of MP appear to be insufficient for cows to calve with adequate protein reserves. Feeding MP at levels of 1100 (cows) to 1400 (first parity) g/d seems to positively influence both production and reproduction.

The amount of time cows spend in a transition group has direct impacts on reproduction, health and production. Assuming the diet is considered an adequate transition diet cows seem to optimize performance when held on this diet for approximately 20 days with no additional benefits beyond this time but reductions in health, production and reproduction if shorter.

Fatty acid nutrition/status has been receiving more attention recently. Mammals have an obligate requirement of Omega-3 and -6 fatty acids as they are used as precursors for signaling factors and hormones throughout metabolism. While we do not know the specific requirements yet, research certainly points to improved fatty acid status prepartum and postpartum associated with better immune function and reproduction.

There are a host of metabolic factors that have been shown to significantly affect reproductive outcomes. Serum albumin (protein nutrition) and cholesterol, NEFAs and BHB (fat and energy nutrition) individually impact reproduction but their interactions may lead to different outcomes. If we superimpose other known factors affecting reproduction (days to first ovulation, disease, body condition, DMI) we begin to see that defining a mechanistic model is feasible. The development of such a model is critical to being able to pinpoint where the largest bottlenecks are to reproductive success in various situations.

Elliot Block Senior Manager, Technology, Arm & Hammer Animal Nutrition, 469 N Harrison St, Princeton, NJ 08540-3510, PH: (609) 279-7517, FX: (609) 497-7176, EM: elliot.block@churchdwight.com

ROLE OF ENERGY METABOLISM IN EARLY LACTATION ON REPRODUCTION

W. Ron Butler, Cornell University

Over the last several decades, large increases in milk production capability among dairy cows have been associated with declining fertility. In high genetic merit cows, feed intake and energy balance begin decreasing in late pregnancy and result in mobilization of body fat as nonesterified fatty acids (**NEFA**) in blood. The onset of lactation after calving is associated with a greater and more prolonged period of negative energy balance (**NEBAL**) during which energy intake lags behind the energy requirements of rapidly increasing milk production. With regard to reproduction during lactation, there is a strong positive association between early commencement of postpartum ovulatory cycles and subsequent pregnancy rate. This important relationship has focused research attention on the regulation and re-initiation of normal ovarian activity in early lactation prior to the breeding period. Energy metabolism, NEBAL, and re-initiation of ovarian activity are inter-connected in dairy cows.

Calving results in an abrupt shift in metabolic demands from net accumulation of body reserves and fetus to rapid mobilization of fat and protein stores for energy metabolism and lactation. Resumption of ovarian activity and early postpartum ovulation depends on the recovery from pregnancy and parturition of important tissues (ovary, uterus, brain and liver). The success of ovarian follicle development for ovulation depends on stimulatory hormonal signals and circumventing the inhibitory effects of NEFA and other NEBAL signals. Follicles begin development during the final weeks of pregnancy when reduction in feed intake and metabolic hormones (Insulin and Insulin-Like Growth Factor, **IGF-I**) become limiting. Insulin resistance in tissues also occurs that affects important liver functions: glucose and IGF-I production and fatty acid oxidation. Collectively, the balance among the energy metabolic signals are linked to responsiveness of the ovary to gonadotropic hormones, thus, determining whether or not developing follicles can produce sufficient estrogen to trigger ovulation. The amount of feed intake during the transition period around calving is crucial to the degree of NEBAL which is the factor most strongly associated with the timing of ovulation (early or delayed).

In dairy cows, the extent of NEBAL becomes visually apparent as loss of body condition and can be scored for comparison between cows. Cows losing greater amounts of body condition during the first two months of lactation will evidence delays in ovulation and lower fertility to artificial insemination during the breeding period. Low fertility in lactating cows delays pregnancy and results in prolonged lactation. When milk yields decline to unprofitable levels, the non-pregnant cows will be culled from the herd.

During early lactation, shifts in energy metabolism regulate the availability of insulin and IGF-I that are key to full development of ovarian follicles producing high levels of estrogen. Not surprisingly, the developmental capacity of oocytes is linked to the growth rate and health of their follicles. There are detrimental effects of early NEBAL on viability of fertilized embryos, but also evidence that energy metabolic effects continue during mid to late lactation in high producing cows *ie.* lactation has a major effect on oocyte/embryo quality. Plasma progesterone levels after ovulation are lower for lactating cows than in non-lactating animals and progesterone affects the uterine environment positively to advance embryo development. *In conclusion, energy metabolism in association with availability of insulin and IGF-I are very important factors related to the low fertility observed in lactating dairy cows.*

W. Ron Butler, Professor and Chairman, Department of Animal Science, Cornell University,
Ithaca, NY 13068 Phone- 607-255- 2862, FAX 607-255-9829, email: wrb2@cornell.edu

Role of Fatty Acids as Nutraceuticals on Reproduction
William W. Thatcher, University of Florida

The current population of high producing dairy cows is sub-fertile. The transitional homeorhetic and homeostatic regulatory responses of the transition and postpartum periods, as cows deal with decreases in dry matter intake, results in a negative energy balance and suppression of the innate arms of the immune system. Cows experiencing periparturient production disorders (e.g., dystocia, metritis, ketosis, hypocalcemia, endometritis) are subsequently less fertile. Targeted strategies of providing specific nutraceuticals that provide pro- and anti-inflammatory effects, such as polyunsaturated fatty acids (e.g., linoleic, eicosapentaenoic/docosahexaenoic, conjugated linoleic acid) provide a means to improve reproductive and lactational performance. Lactating dairy cows receiving supplemental dietary lipids beginning in the pre-calving transition diet or early postpartum have metabolic and hormonal responses that complement recrudescence of ovarian activity and subsequent fertility. Transition period feeding of lipid supplements enriched in n-6 fatty acids, such as calcium salts of safflower oil, increases neutrophil phagocytosis of bacteria and killing activity, enhances neutrophil production of cytokines such as TNF-α and IL-1β, as well as increasing acute phase proteins such as haptoglobin and fibrinogen. These pro-inflammatory responses improve overall cow health contributing to an increase in milk production. Feeding calcium salts of fish oil (FO) from 30 days postpartum through the breeding period exerted anti-inflamatory responses on neutrophil function,improved pregnancy/AI and reduced pregnancy losses. The greatest reproductive advantage was observed in cows sequentially fed lipid supplements containing calcium salts of safflower oil followed by FO during the postpartum breeding period. Mechanistic studies dealing with gene expression of the endometrium in response to feeding FO indicated that FO treatment in cyclic lactating dairy cows complemented pregnancy effects at day 17 after the preovulatory induced LH surge. The FO treated cyclic cows (with or without bST injections) had reduced staining intensity of PGHS-2 protein in the luminal epithelium compared to Control cyclic cows (with or without bST injections). Furthermore, FO treated cyclic cows (without bST) had reduced moderate to heavy staining intensity for Estradiol Receptor Alpha in the luminal epithelium; within the superficial glandular epithelium, FO increased the amount of moderate and heavy staining for the nuclear progesterone receptor. These FO-mediated effects in cyclic cows are similar to the responses of pregnancy in response to the conceptus, and it is hypothesized that such synergistic effects would contribute to greater survival of embryos or maintenance of pregnancy. Feeding Ca salts enriched in omega-6 and *trans* fatty acids during transition and postpartum periods improved both embryo development and pregnancy per AI. Furthermore feeding of *trans*-10, *cis*-12 conjugated linoleic acid to postpartum dairy cows increased the probability of earlier postpartum ovulations that contributed to a greater accumulation of pregnancies such that the median time to pregnancy was decreased to 105 DIM, which was 38 d less than for cows receiving no CLA (143 DIM). Collectively, the above findings indicate that selective supplementation with polyunsaturated fatty acids during key physiological periods improves postpartum immune responses and reproductive performance.

Dr. William W. Thatcher
Department of Animal Sciences
IFAS, University of Florida
Gainesville, FL 32611-0910; Thatcher@ufl.edu