A New Perspective on Management of Reproduction in Dairy Cows: the Need for Detailed Metabolic Information, an Improved Selection Index and Extended Lactation

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Abstract. For lactating dairy cows, we need management tools, that are “clean, green and ethical”, cost-effective and easy to use. Specific tools are needed for artificial insemination (AI) after oestrus detection within a few months of calving, and for managing the complex nutritional requirements of cows between successive calvings. Assessment of energy deficit by measurement of body condition score (BCS) has been useful in the past but we now need more sophisticated ways to measure the relationship between adipose tissue and fertility. For this reason, we have focused our attention on the cells of the adipose tissue, the adipocytes, and the role of the hormone that they produce, leptin. This hormone affects pulsatile LH release and, in dairy cows, it seems to be linked to the first postpartum ovulation. Adipocytes are always sensing energy status and they control leptin secretion dynamically, so blood leptin concentrations can change acutely, even when there is no detectable change in BCS. Leptin secretion seems to be determined by the secretory activity of each adipocyte as well as the total mass of adipocytes in the body of the animal (as measured by BCS). The strong relationship between BCS, leptin concentration and reproductive function in dairy cows suggests that we should reconsider the interval of the recovery from prepartum and postpartum damages, the need for high milk yields at the last lactation causing the dry-off stress and the subsequent troubles. We should also re-assess the current drive to reduce calving interval because milk yields during the early stages of lactation are economically very important but high yields seem to cause several metabolic and reproductive disorders in modern dairy cows. In general, the thinking has been that calving interval must be short because short intervals are more profitable. However, if we remember that main product from dairy cows is milk and that a short calving interval is very difficult without reproductive problems, then a longer calving interval might be more sensible and also more profitable. We have example of an extended calving interval in Japan, Supercows which are very rare cows yielding remarkable high milk. Finally, we probably need to improve dairy cows genetically if we are to achieve the goal of “clean, green and ethical” dairy farming. This paper reviews data relevant to these strategies and we conclude that more basic and applied research will be required if we are to find ways to reach that goal.

Key words: Postpartum recovery, Calving interval, Adipocyte, Leptin

which seem to be linked to reproductive failures such as the failure of pregnancy [1]. Clearly, we need new management tools that are cost-effective and easy to use for farmers. At the same time, we should aim for tools that are “clean, green and ethical”: non-hormonal and non-chemical treatments (clean), increased use of roughage and decreased use of concentrate in a more sustainable system (green), with animals that are calm and healthy (ethical). Management systems developed along these lines would greatly improve the image of our meat and milk industries in society and thus in the market place. “Clean, green and ethical” dairy farming may also make good business sense: for example, the price of 1 L of normal milk in Japan is about 200 yen but milk with a “clean, green, and ethical” image can be sold for 770–1000 yen per litre.

In this paper, we consider “clean, green, and ethical” ways to improve the management of dairy cows that are bred by for artificial insemination (AI) after oestrus detection by humans, generally only a few months after calving, and that have complex nutritional requirements between successive calvings. We will address 1) Metabolism, 2) Genetics and 3) Extended lactation.

**Metabolism: Relationship between Body Condition Score in the Periparturition Period and Postpartum Metabolic Disease and Reproductive Function**

Dairy cows in early lactation are in negative energy balance because they require more energy than they can obtain from their dietary intake. In this situation, the cows rely on the mobilization of adipose reserves and they often lose 60% or more of their body fat in the first few weeks after parturition [2]. Management of the prepartum period is very important for controlling this problem because high body condition score (BCS) at calving leads to a greater loss of BCS loss after calving and thus a lower postpartum BCS. This excessively rapid mobilization of fat early in the postpartum period is a major risk factor for prolonged anovulatory periods, and the delay to the beginning of recovery of energy balance after parturition is positively correlated with the delay from parturition to first ovulation. The marked loss of BCS (1.0–1.5 points on a 5-point scale) from the dry to near calving periods increases the occurrence of postpartum metabolic and reproductive diseases, extends the interval to first breeding after calving, lowers the likelihood of pregnancy after breeding, and significantly increases the number of days open. Even the “Ovsynch Timed AI” protocol cannot improve the pregnancy rate in low BCS cows—in order to obtain good conception rates after this treatment at 8 weeks postpartum, dairy cows must have a normal BCS on both 30 d postpartum and during the days of “Ovsynch” [3].

A one unit reduction in BCS from calving to 30 days postpartum causes more than double the rate of pregnancy loss in lactating dairy cows [4], and the extent of embryonic loss is greater in cows that lose body condition in early gestation [5]. The mechanism for this failure of pregnancy with BCS loss is not yet fully understood but, as we discuss below, loss of adipose tissue loss is the one of important factors. Another possible factor is the quality of oocytes, because the cleavage and blastocyst formation rates are greater for oocytes from cows with high BCS than from cows with low BCS [6], as reviewed by another paper in this issue.

The strategy of feeding more concentrates so as to increase energy supply has resulted in adverse effects on health and reproduction, because the cows eat as much as possible and the high energy density of the feed can easily induce diarrhea and anorexia. Even when these diseases are not detectable externally, the excess concentrate may harm reproductive function because of abnormal uterine pH or excess ammonia. One better strategy, that also happens to be “green”, is to feed good quality roughage, but restrict the ratio of dry matter intake to the body weight remains a most important and insurmountable difficulty that affects the balance among milk production, BCS loss and health in postpartum dairy cows. Previous attempts to reduce the interval to commencement of luteal activity postpartum (CLA) by manipulating nutrition during postpartum period have provided equivocal results (e.g., with fats, calcium salts of long-chain fatty acids, propylene glycol). In general, results from manipulating nutrition are variable and not cost effective, and it is not clear whether results obtained under experimental conditions can be replicated in large-scale field trials, because the responses will be significantly influenced by variation between herds. No matter how we look at it, postpartum
reproduction in high-producing dairy cows is a very difficult issue.

Leptin and pulsatile LH secretion in dairy cows around parturition and postpartum first ovulation

The delay to the beginning of recovery of energy balance after parturition is positively correlated with the delay from parturition to first ovulation, and it is thought that this relationship is mediated by insulin-like growth factor-I (IGF-I) [7]. However, based on the reports in recent years, it seems unlikely that a single hormone or energy substrate is responsible for linking the nutritional status of animals to their reproductive function. Another candidate is leptin, a cytokine-hormone secreted mainly by adipose tissue that has been proposed to act as a direct metabolic signal to the sites in central nervous system that control pulsatile LH release [8]. It seems very likely that leptin accompanies IGF-I in controlling the resumption of ovulation.

This led us to study the relationship between plasma leptin concentrations and the timing of the first ovulation postpartum in Holstein dairy cows [9]. Leptin concentrations declined after parturition and, after reaching a nadir, they increased and became stable near the time of first ovulation. The delay to first ovulation was correlated with the interval from parturition to the leptin nadir, suggesting that a delay in the recovery of leptin secretion increases the delay to the first ovulation. Other studies found that leptin levels are low during the early postpartum period, when LH pulses are likely to be inhibited [7] because GnRH neuronal activity is suppressed by various neurotransmitters, such as opioids [10]. The decline in leptin production is likely to be due in part to the negative energy balance [11]. In other animal models, a stimulatory effect of leptin on pulsatile LH secretion has been detected in monogastrics or ruminants when they are under severe energy shortage [12], but not under slight or no energy shortage. Together, these observations suggest that there should be a direct relationship between pulsatile LH release and leptin concentrations in Holstein dairy cows during the postpartum period before the first ovulation. We have tested this hypothesis, and also considered other parameters related to energy status. We found that LH pulse frequency was positively correlated with energy balance and with plasma concentrations of leptin, and that LH pulse amplitude was correlated only with leptin values (unpublished data, Fig. 1). In rats, fasting prolongs postpartum lactational anoestrus and this effect is prevented by both central and peripheral leptin administration [13]. Thus, there seems to be a strong physiological link between leptin production and the reproductive axis, the most obvious possibility being a role for leptin in the control of pulsatile LH secretion, a major factor in the ovulatory process.

Other studies [8, 14, 15] also support our contention that more than one hormone and energy substrate are responsible for the linkage between nutritional status and reproductive function. Thus, we should image multifactorial model, for example, Liebig’s Law of the Minimum.

Mechanisms controlling blood leptin concentration in ruminants

In ruminants, circulating leptin concentrations are positively correlated with body fatness, but this relationship only explains about 10–30% to the
variation in plasma leptin concentration, so other factors must playing important roles. Among those factors is feed intake.

In mice and humans, it is clear that glucose stimulates leptin secretion but, for ruminants, there are few comparable studies. Kauter et al. [16] reported that plasma leptin levels in sheep did not respond in the short-term (2 h) to a single intravenous injection of glucose and our own observations agree [17]. However, in our study [17], we observed postprandial increases in leptin concentration, and the glucose infusion maintained the high leptin levels, in contrast to the sheep infused with saline where there was a decrease after the postprandial peak. Thus, glucose itself may not affect leptin secretion from ruminant adipocytes, but it is possible that there are indirect effects induced by glucose infusion or by volatile fatty acids (VFA) may stimulate the leptin secretion.

Fasting decreases plasma leptin levels sharply in sheep and cattle, and refeeding reverses the effect [18, 19]. However, in dry, non-pregnant ewes, the response to refeeding was found to be strongly dependent on the nutritional history of the animals: it was much higher in fat than in lean ewes and, for a given level of body fatness, it was lower in previously underfed than in previously well-fed ewes [19].

In cows, intravenous infusions with glucose can increase blood leptin levels in mid-lactation but not in early lactation [19]. Refeeding after fasting increase the blood leptin concentration in sheep, and the hyperglycemia and hyperinsulinemia enhance such leptin increase after the refeeding. However, the positive effect of oral treatment with VFA-like glucogenic formulation is blunted in the pregnant cows immediately before parturition [20]. Thus, the late stage of gestation and early stage of lactation affect leptin secretory activity. Interestingly, cows selected for a high milk fat content had higher glucose uptake by insulin-sensitive tissues and higher plasma concentrations of leptin [19].

Therefore, leptin secretion is regulated in the short, mid- and long term by feed intake, nutrients and hormones (especially glucose and insulin), by feeding level, energy balance, physiological stage, and also by body fatness, a reflection of the nutritional history of the animals. Leptin could play a role as integrator of the animal’s energy requirements. Conversely, the leptin response to nutritional treatments that aim to improve reproductive performance should depend on both the recent and more long-term history of the nutritional status of the animal. Furthermore, the combination of data for current BCS and BCS history, feeding and the physiological cycle of the animal, will be better than current BCS alone, as a cheap, easy method for estimating the effect of nutritional status on the reproductive function.

Genetics: The Need for Genetic Improvement of Dairy Cattle in Japan

Long-term emphasis on selection for milk yield, combined with its antagonistic genetic correlation with female fertility, has resulted in a reduced capacity of dairy cows to conceive and carry a calf to term. Incorporating genetic evaluations for fertility traits into breeding programs could solve the problem. However, Miglior et al. [21] reported that the Japanese selection index, Nippon Total Profit (NTP), has no direct emphasis on health or reproduction, in contrast to the relatively strong emphasis on these traits in the national selection indices of the other 15 countries who are members of International Bull Evaluation Service (INTERBULL). The accuracy of genetic evaluation depends on the heritability of each trait, but the heritabilities of most fertility traits (e.g., calving interval, days open, pregnancy rates) are quite low (< 0.05), due to large contributions by non-genetic factors, such as differences among cows, AI technician and management protocols. This explains the lack of direct emphasis on health and reproduction in the Japanese index that we must begin to consider upgrading.

One possible strategy is to develop a completely new selection system. Schneider et al. [22] reported that the breeding value of sires may be predicted accurately with a model that includes “survival analysis” using the intervals from parturition to conception in daughters. Survival analysis is a statistical method that evaluates the timing of events and calculates the probabilities for each time interval. It is particularly useful for survival, but can also be used for other non-recurrent events occurring in a cohort over time (e.g., relapse, death). Because almost all dairy cattle in Japan are bred by artificial insemination, it is feasible to
Another strategy is to use traits with higher heritability, more readily available records, and good genetic correlations with fertility to reduce the risk of reproductive difficulties in cows. Among these are milk fat and protein yields, BCS loss, and BCS changes [23–25]. We must cautious because higher milk fat means good energy balance after mid-lactation, but it means energy shortage during the early postpartum period because milk fat content is increased during the mobilization of body fat. We could also use endocrine measures of fertility [26] and incorporate them into an index that will improve the accuracy of prediction of breeding value for fertility. With further study, we may find other valuable parameters based on endocrinology and molecular biology.

Snijders et al. [6] reported that cows of high genetic merit had higher milk production, greater loss of body condition between calving and first service, and also lower conception rates (to first and second service, and overall). They thus required more services per conception than cows of medium genetic merit, but reproductive performance was not associated with either milk production or feed intake. Thus, if we begin genetic improvement for both milk production and fertility and we develop better methods for management, we should be able to obtain good reproductive performance even from high-producing dairy cows.

There is significant between-animal variation in the responses to manipulating nutrition. This is an important problem because it makes it difficult for farmers to use a uniform management strategy for all cows in the same herd, despite the contribution of information technology (IT) and electronic identification systems (e.g., IC tag). One of the main factors involved is the predisposition of some individual cows to partition nutrients to milk production rather than body tissues and the ability of others to increase dietary intake in parallel with increasing milk yield. Genetic improvement should to reduce this variation among cows, or increase the adaptability of cows to various nutritional factors. This would help us to achieve the goal of ‘clean, green and ethical’ dairy farming.

Extended Lactation: Fine Tuning the Calving Interval—a Possible Strategy for Clean, Green and Ethical Dairy Farming

It is generally accepted that 12-month calving intervals are the most profitable, based on the shape of the lactation curve and the perceived costs of extended lactations. However, these fundamentals have now been challenged and the best cows can maintain high milk yields for a much longer period of lactation than was previously considered normal. Because milk yields during the early stages of lactation are economically very important, we should reconsider the need for maintaining high milk yields at the beginning of the dry period. Furthermore, we should also reassess the current drive to reduce calving interval. Veerkamp et al. [27] reported high genetic correlations between the interval to first ovulation postpartum and yields of milk ($r=0.51$), fat ($r=0.65$) and protein ($r=0.48$). Thus, the delayed recovery in modern dairy cows may have been programmed in their genome.

Although short calving intervals are seen as more profitable, we must remember that main product from dairy cows is milk, and the strategy of extended calving interval may be one good option for dairy farmers. For example, in Israel, Arbel et al. [28] examined the effect of a 60-day longer voluntary waiting period before the beginning of inseminations and the extended calving interval on production and profitability of high yielding cows. They found no significant decrease in daily milk yield but, importantly, they observed economic advantages in cows with extended lactations. Other reports from Sweden [29] and Australia [30] also concluded that extended lactations are a suitable option for some enterprises, and that suitability will depend on various factors, particularly cow milk production and especially persistency (the rate of decline in milk yield from peak), as well as management.

We need to be aware of the genetic variation among cows, even within the same herd. The most appropriate calving-to-calving interval depends on genotype, environment and the interaction between genotype and environment [31]. In addition, we need to aware of the phenotypic diversity of the fertility traits; for example, the interval from calving to first ovulation postpartum, and the interval from calving to conception are log-
normally distributed, not normally distributed. Thus, the countermeasures should be determined after considering both the distribution curve of the target and the criteria for the cutoff.

Persistency is most important factor determining the most appropriate calving interval, for both enterprise profit and cow health. For example, if the milk yield before the dry is too low and the cow becomes fat, there is an increased risk of both metabolic disease around the subsequent calving and reproductive failure at the next parity. In addition, for the same reasons, we must avoid the decreasing BCS during the dry period and we should tune BCS during the last lactation period by changing the dense energy ration and milking frequency. On the other hand, if milk yield before the dry is too high, there is likely to be an increased risk of liver damage after the dry, as described in another review in this issue. Pregnancy has a deleterious effect on persistency, but milk production decreases only after about Day 150 of gestation due to an as yet undefined mechanism [32, 33]. Importantly, persistency is a heritable trait and could be a target for selection.

Thus, in Japan as in other countries, we need to reassess whether higher milk yield plus shorter calving interval is always the most profitable combination. One parameter of reproductive efficiency in dairy cows that is used in Japan is 1,200 yen per day of delayed conception, but 60 days of delayed AI does not necessarily cause a loss of 72,000 yen in modern lactating cows. Rather than operate on the basis of this simplistic relationship, farmers should choose a calving interval on the basis of scientific judgment.

The use of extended lactation in Japan will be helped by animals like the “Supercow”, currently a very rare cow that has a remarkably high yield. Examples are shown in Fig. 2: one cow produced for 612 days at her first parity and 568 days at her second (Fig. 2a). The second “Supercow” produced for more than 900 days in her fourth parity (Fig. 2b). A third Supercow (not shown) produced 16,127 kg milk for 456 days at her first parity, then, between her second and seventh parities inclusive, produced milk for 365 to 572 days (yields ranging between 18,505 kg and 34,102 kg).

Fig. 2. The lactation curves of “Supercows”, very rare cows with remarkably high milk yields. a) A “Supercow” that produced 18,693 kg of milk in 612 days of her first parity, and 26,473 kg of milk in 568 days of her second parity. b) A “Supercow” that produced more than 32,000 kg of milk in more than 915 days of her fourth parity.

Conclusions

We need to accept that modern dairy cows have always been changing and always will, and management strategies should be upgraded according to those changes. We also need to upgrade our selection index so can continue to improve dairy cows genetically, in order to increase “easy” cows, if we are to achieve the goal of “clean, green and ethical” dairy farming. At the same time, we must remember the various biological limits of these large animals, such as the need for time to recover from the impact of peripartum events, the roughage-concentrate ratio for a healthy rumen and
other parts of body. Furthermore, we should remember that hooves and legs of cows have a biological limit for carrying weight, so maximum values for body weight, feed intake and milk production need to be reconsidered. We should give the cows some margin in these parameters for their health and reproduction. In addition, we need to remind dairy farmers that high profits can only be gained by excellent collaboration between humans and cows, never from poor management of excellent cows. Finally, we need more basic and applied research if we are to draw a road map that will allow us to reach the goal of “clean, green and ethical” dairy farming.

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