

ADSA Foundation Scholar Award

Reproductive Loss in High-Producing Dairy Cattle: Where Will It End?¹

M. C. Lucy

Department of Animal Sciences,
University of Missouri, Columbia 65211

ABSTRACT

The dairy industry in the United States has changed dramatically in the last decade. Milk production per cow has increased steadily because of a combination of improved management, better nutrition, and intense genetic selection. Dairy farms are larger, and nearly 30% of the dairy cows in the United States are on farms with 500 or more cows. The shift toward more productive cows and larger herds is associated with a decrease in reproductive efficiency. Cows with the greatest milk production have the highest incidence of infertility, but epidemiological studies suggest that, in addition to milk production, other factors are probably decreasing reproductive efficiency in our dairy herds. The reproductive physiology of dairy cows has changed over the past 50 yr, and physiological adaptations to high milk production may explain part of the reproductive decline. Critical areas for new research include control of the estrous cycle, metabolic effects of lactation on reproduction, mechanisms linking disease to reproduction, and early embryonic mortality. Solving reproductive loss in dairy cows will not be easy because only a small number of research groups study reproduction in postpartum dairy cows. Therefore, the present research base will need to be expanded. For this to occur, research funding must be increased above its current level and a renewed emphasis must be placed on solving the emerging crisis of infertility in dairy cows.

(**Key words:** dairy cow, reproduction, ovary, lactation)

Abbreviation key: CL = corpus luteum, NIH = National Institutes of Health, NRICGP = National Research Initiative Competitive Grants Program.

INTRODUCTION

The rapid progress in genetics and management in the dairy industry throughout the world has created a

new era in which a smaller number of dairy cows meet the growing demand for dairy products. To meet the demands of the 21st century, individual cows produce more milk and are found on farms with larger herd sizes. Milk production of individual cows depends on their ability to become pregnant because the lactation cycle is initiated and renewed by pregnancy (with the obvious exception of induced lactation). In an effort to gain the greatest efficiency and lifetime productivity, dairy cattle are inseminated and pregnancy is established while dairy cows are lactating. Gestation and lactation overlap until the dry period before the next lactation. Therefore, there is an inherent requirement to establish pregnancy in lactating dairy cows. The modernization and consolidation of the dairy industry during the past quarter century has created many new challenges. One challenge that will undoubtedly affect future efficiency of the dairy industry is the decline in fertility and reproductive efficiency in modern dairy cows. The root cause of the declining fertility is probably a combination of a variety of physiological and management factors that have an additive effect on reproductive efficiency. Although the relative contribution of individual factors leading to infertility can be debated, the cumulative effect (infertile cows) erodes the efficiency and profitability of the dairy industry.

CURRENT STATUS OF REPRODUCTION IN DAIRY COWS

The first question that must be answered is whether the perceived decline in reproductive efficiency actually exists. A number of recent publications have documented the decline in reproductive efficiency. For example, Butler (1998) presented data showing a decline in first-service conception rate from approximately 65% in 1951 to 40% in 1996 (New York dairy cattle) (Figure 1). An examination of the literature published in the *Journal of Dairy Science* confirms this trend. For cows inseminated artificially at observed estrus, investigators in the 1950s typically reported conception rates of approximately 55% (Casida, 1961). The published conception rates in recent journal articles are approximately 45% for inseminations at spontaneous estrus

Received August 23, 2000.

Accepted January 26, 2001.

E-mail: lucym@missouri.edu.

¹Contribution from the Missouri Agricultural Experiment Station Journal Series No. 13,109.

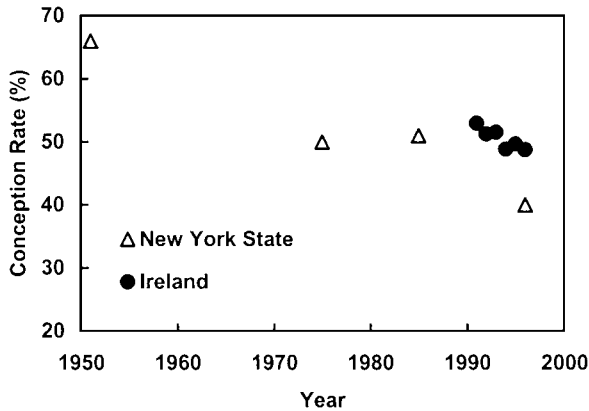


Figure 1. Yearly averages for conception rate to artificial insemination for lactating dairy cows in either New York State (United States; Butler, 1998) or Ireland (O’Farrell and Crilly, 1999) during the past half-century.

(Dransfield et al., 1998) and approximately 35% when timed AI is used (Schmitt et al., 1996; Pursley et al., 1997a, 1997b, 1998).

Declines in reproductive efficiency in dairy cattle are not only occurring in the United States. Equivalent decreases in first-service conception rate have been reported in Ireland (Roche, 2000), the United Kingdom (Royal et al., 2000), and Australia (Macmillan et al., 1996). Factors causing reproductive decline in Europe and Australia may be different from those in the United States. For example, the rapid adoption of North American genetics and the associated increase in milk production in countries that depend heavily on grazing (instead of TMR feeding) may create a situation in which North American genetics are not matched with local management and feeding practices (Macmillan et al., 1996). Nevertheless, poor reproductive efficiency is a worldwide problem affecting the dairy industry.

The extent of reproductive decline being experienced by dairy producers is not well documented. Several investigators have summarized DHIA records and shown trends for worsening reproductive performance in dairy herds. For example, Silvia (1998) summarized records from dairy herds in Kentucky and reported an increase in services per conception of 1.62 to 2.91 from 1972 to 1996. We observed increasing services per conception, days open, and days to first insemination in 143 dairy herds continuously enrolled in the DHIA record system from 1970 to 1999 (personal communication, J. S. Clay, Dairy Records Management Systems, Raleigh, NC). Milk production (rolling herd average) steadily increased throughout the study period. The greatest reproductive decline, however, occurred after the mid 1980s (Figure 2). Although dairy record centers provide voluminous data on the problem, the owners of the

represented herds must make a voluntary decision to enroll in a dairy testing program, and, therefore, the data do not represent a random sample of all US dairy herds. The actual numbers for all herds may be slightly better or worse than those reported in Figure 2.

There is an obvious need for national studies of reproduction in US dairy cows so that the causes of reproductive decline can be identified. In response to dairy farmer concerns, the Australian Dairy Research and Development Corporation (Melbourne, Australia; <http://www.drdc.com.au>) commissioned a study to determine the extent of reproductive decline in Australian dairy herds and the root causes of the problem (the InCalf project). The study began in 1995 and involved 33,000 cows from 168 herds. Veterinarians interviewed farmers and collected detailed records on each cow in the study. The data set was more extensive than what might be typically available through dairy herd record centers in the United States. The results were then summarized and are being published in booklets that are designed to answer practical questions about dairy reproduction. For example, what effect do calving-related problems and milk production have on interval to conception (Table 1)? Although the scientific literature may contain those data for US dairy cows, the numbers are not readily accessible to producers who would most likely use the information for management decisions. Similar studies in the United States would be extremely valuable as we attempt to manage and make recommendations for dairy producers in the 21st century.

Is Reproductive Decline Caused by Greater Milk Production?

Milk production for United States Dairy cows has increased by approximately 20% in the last 10 yr (USDA

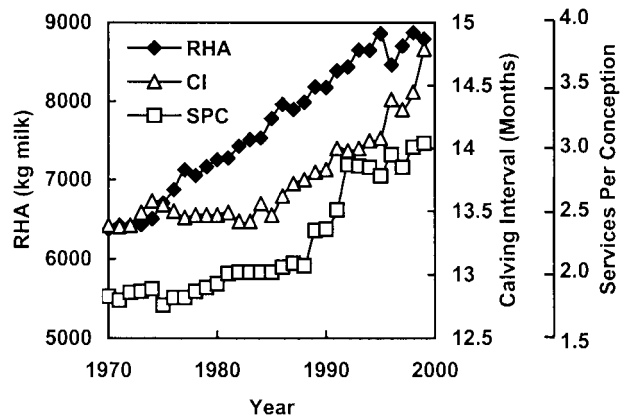


Figure 2. Rolling herd average (RHA, kg milk per lactation), calving interval (CI), and services per conception (SPC) for 143 dairy herds continuously enrolled in the Raleigh DHIA record system from 1970 to 1999 (personal communication, J. S. Clay, Dairy Records Management Systems, Raleigh, NC).

Table 1. Results for continuous calving herds enrolled in the InCalf Project of the Australian Dairy Research and Development Corporation (Melbourne, Australia; <http://www.drdc.com.au>).

Condition or production level	Number of cows	100-d in-calf rate ¹ (%)	200-d not-in-calf rate ² (%)
Dystocia			
Not affected	27,713	58	10
Affected	1,749	51	14
Twin calving			
Not affected	29,070	58	10
Affected	392	43	10
Retained placenta			
Not affected	28,132	59	10
Affected	1,330	46	15
Vaginal discharge			
Not affected	29,188	58	10
2 wk or less after calving	105	45	0
2 to 4 wk after calving	83	50	40
More than 4 wk after calving	86	34	43
Milk volume (liters)			
4,000 or less	3,102	56	11
4,000 to 6,000	13,781	57	9
6,000 to 8,000	10,019	58	8
More than 8,000	1,888	57	9

¹Percentage of cows that became pregnant by 100 d after calving.

²Percentage of cows that had not become pregnant by 200 d after calving.

National Agricultural Statistics Service; <http://www.usda.gov/nass>). At the same time, indices of reproductive efficiency have worsened (Figure 2). From these data, an intuitive association between greater milk production per cow and deteriorating reproduction has been made. There is a long history of associating greater milk production with reduced reproductive performance in dairy cattle. In a recent review of the genetics of modern dairy cattle, Hansen (2000) cited a quotation from a 1929 Minnesota Agricultural Experiment Station Bulletin that demonstrated the perception of poor reproductive performance in high-producing dairy cattle. Based on the analyses of large datasets, there is clearly an antagonistic relationship between milk production and reproduction in dairy cattle (Dematawewa and Berger, 1998; Hansen, 2000). However, the effects of increased milk production on reproduction are relatively minor compared with the effects of other factors. For example, in their recent paper on the epidemiology of reproductive performance in dairy cows, Gröhn and Rajala-Schultz (2000) reported that the hazard ratio for cumulative first 60-d milk yield was near 1.0 (i.e., neutral effect) for most levels of milk production in US Holsteins. Only at the highest level of milk production was there a nonsignificant increase in hazard ratio. More important factors for conception were season of calving and postpartum disease (Table 2). The InCalf study of Australian dairy cows (Table 1) as well

as other studies of European dairy cows (Loeffler et al., 1999a) reached similar conclusions about the relative effects on conception of milk production versus disease (i.e., minor effects of milk production on conception; greater effects of disease than level of milk production).

Summaries of reproductive records for herds of different levels of production also suggest negligible effects of milk production on reproductive efficiency. In fact, higher producing herds generally have better reproductive performance (Nebel and McGilliard, 1993; Stevenson, 1999). The improved reproduction in high-producing herds probably reflects better feeding, healthier cows, and better reproductive management. A close examination of the Raleigh DHIA data sets of Nebel and McGilliard (1993) and Stevenson (1999), however, shows a surprising change in reproductive statistics from 1992 to 1999. Although both investigators stratified herds within comparable levels of production, the reproductive statistics were considerably worse for herds at a given level of production in 1998 to 1999 (Stevenson, 1999) relative to herds at the same level of production in 1992 (Nebel and McGilliard, 1993). Clearly, factors in addition to increased milk production are decreasing reproductive efficiency in US dairy cows.

High milk production should not be confused with negative energy balance. Cows undergo a normal process of nutrient partitioning and adipose tissue mobilization during early lactation (Bauman and Currie, 1980). Negative energy balance, weight loss, and decreased BCS occur during early lactation when nutrient re-

Table 2. Effect of milk yield and disease on hazard ratio for conception in 13,307 New York State Holstein cows (Gröhn and Rajala-Schultz, 2000).

Production level, calving months or disease	Hazard ratio ¹
First 60-d cumulative milk yield (kg)	
≤ 1582	1.0
1583 to 1891	0.99
1892 to 2195	1.01
2196 to 2641	1.01
> 2541	0.92
Calving months	
December to February	1.0
March to May	0.93*
June to August	1.06
September to November	1.01
Disease	
Retained placenta	0.86**
Metritis	0.85**
Ovarian cysts	0.79**

¹The hazard ratio is the relative risk of conception. A hazard ratio of 1.0 equates to a neutral effect. Hazard ratios less than one indicate reduced likelihood of conception (i.e., cows experiencing a disease with a hazard ratio of 0.86 are 14% less likely to conceive compared with a healthy cow).

* $P < 0.05$.

** $P < 0.01$.

quirements for maintenance and lactation exceed the ability of the cow to consume energy in the feed. The highest-producing cows in the herd are not, however, necessarily those with the greatest negative energy balance or the lowest BCS. In studies of Illinois dairy cattle, greater DMI in high-producing cows compensated for greater milk production, so that energy balance was similar in high- and low-producing cattle. Low-producing cows with poor DMI were at greater risk for anestrus and infertility than were high-producing cows (Lucy et al., 1992; Staples et al., 1990).

Epidemiological studies suggest that disease parameters (e.g., ketosis, mastitis, retained placenta, and cystic ovary) have a greater effect on herd fertility compared with nondisease parameters (e.g., milk production and BCS). Loeffler et al. (1999a), however, point out that disease parameters affect a lesser percentage of the herd than do nondisease parameters. Therefore, the modest effects of milk production on fertility are important because every cow in the herd is affected. A greater understanding of the physiological basis for the antagonistic relationship between milk production and fertility is needed. Once the basis for the relationship is known, then feeding or management strategies can be implemented to counteract the effects of greater milk production on reproduction. This would partially correct the current decline in dairy reproduction. Other factors will need to be addressed, however, before declines in dairy reproduction are reversed.

What Other Factors Could Explain Deteriorating Reproduction In Dairy Cows?

Several studies suggest that the effects of milk production on reproduction can only be observed in highest-producing dairy cows. Perhaps the recent declines in reproduction simply reflect greater percentages of US dairy cows within the high-producing category. Based on improved milk yields, the trend for poorer reproduction caused by greater milk production will continue and will theoretically worsen as cows achieve greater production. Other changes within the dairy industry, however, probably have equivalent or greater effects on reproduction in dairy cows. The relative contributions of the various physiological, genetic, environmental, and management factors toward the decline in dairy reproduction are not known. Some of the factors that are potentially affecting reproduction in dairy cattle are discussed below.

The number of milk cow operations in the United States is decreasing for all herd classifications with fewer than 200 cows (Figure 3). At the same time, the number of herds with more than 200 cows is increasing. The most recent USDA National Agricultural Statistics

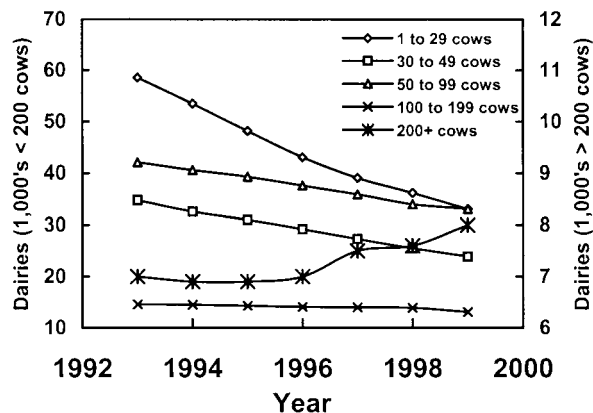


Figure 3. Number of United States dairy farm operations with different herd sizes from 1993 to 1999 (USDA National Agricultural Statistics Service; <http://www.usda.gov/nass>).

Service survey showed that nearly 30% of all dairy cows in the United States were found on farms with more than 500 cows. Therefore, the trend in US dairying is toward consolidation of the dairy industry into large farms with more than 500 cows. Stahl et al. (1999) studied 50 Minnesota herds that increased milk output by 90%. The herds increased output by adding cows. At the same time, the use of free stalls, milking parlors, and full- and part-time hired labor increased. Fifty-two percent of growth was achieved by purchasing pregnant heifers that later calved and had their first lactation on the farm.

The study of Stahl et al. (1999) demonstrated that first-lactation cows are often used for herd expansions. First-lactation cows have lower energy balance because they eat less and have energy requirements for growth in addition to lactation. Lower energy balance in first-lactation cows was associated with delayed intervals to first ovulation (Lucy et al., 1992), and this may explain why some studies have identified first parity as a risk factor for conception failure at first AI (Loeffler et al., 1999b). In addition to herd expansions, first-lactation cows also represent a larger percentage of the herd when cow turnover is increased by infertility in older cows. Expanding herds or herds with fertility problems, therefore, may have decreased herd reproductive efficiency because a greater percentage of the herd consists of first-lactation cows whose reproduction may inherently be compromised.

The shift in herd size toward larger dairies creates a new paradigm for reproductive management. Traditional methods of visual estrus detection followed by AI may serve the modern dairy industry poorly when cows are managed in large groups. Although the exact contribution may be impossible to quantify, some of the decrease in reproductive efficiency in dairy farms may

be attributed to “growing pains” as dairies expand and attempt to manage reproduction with methods developed for smaller herds. Large herds require more time for heat detection, identification, sorting, insemination, and record keeping simply because there are more cows. In some herds, nonelectronic estrus detection aids (e.g., tail chalk, patches) have replaced visual detection of estrus and cows are inseminated based on rubbed tailheads, activated tail patches, or the appearance of vaginal mucus. The responsibility for reproduction also falls on employees (instead of the owner) who may be overwhelmed by the number of cows that they manage. The inherent problems of attracting and keeping high quality labor on dairy farms may have been compounded by low US unemployment throughout the 1990s (United States Department of Labor, <http://www.dol.gov>).

Larger herd sizes are creating the need for new approaches to reproductive management. A recent survey from the Hoard's Dairyman Research Department (Fort Atkinson, WI) indicated that approximately 10% of US dairy herds use timed AI for breeding dairy cows. Timed AI programs are popular because herds with poor estrus detection rates can achieve superior intervals to first insemination and pregnancy compared with cows inseminated at an observed spontaneous estrus (Pursley et al., 1997a, 1997b, 1998; Schmitt et al., 1996). Timed AI programs offer acceptable pregnancy rates (pregnant cows/all cows) without estrus detection. Dairy cows inseminated within timed AI programs, however, have a lower conception rate (pregnant cows/inseminated cows) compared with dairy cows inseminated at an observed spontaneous estrus (Nebel and Jobst, 1998). Therefore, traditional reproductive indices such as services per conception and conception rate are negatively affected when timed AI is implemented. Interval to first service and overall pregnancy rate may, however, be improved.

Herd health has a large effect on herd reproduction. Moving cows into confinement housing and managing cows in larger herds increases the risk of mammary and uterine infections (Goldberg et al., 1992; Kaneene and Miller, 1994). Mammary and uterine infections are risk factors for infertility in dairy cows (Emanuelson and Oltenacu, 1998; Loeffler et al., 1999a, 1997b; Risco et al., 1999). If cows housed in large confinement herds have more disease, then their fertility will be lower.

Administration of recombinant bST to dairy cows is now an accepted and widely used management practice that increases milk production (Bauman, 1999). Administration of recombinant bST also causes a modest decrease in reproductive performance (Cole et al., 1991). In a large study involving 28 dairy herds, recombinant bST administered to primiparous cows caused a 16-d

increase in days open but did not affect overall pregnancy rate (Collier et al., 1997). In the same study, days open in multiparous cows were not affected, but the pregnancy rate of multiparous cows was decreased by 7 percentage points. The widespread use of recombinant bST for the purpose of increasing milk production in US dairy cows may be influencing national statistics for dairy reproduction. In their study of 340 herds, however, Bauman et al. (1999) concluded that bST did not affect stayability or herd life of dairy cows. Furthermore, the current period of reproductive decline (Figure 2) began well before the introduction of bST in 1994, and countries in which bST is not used (Ireland, the UK, and Australia) are experiencing reproductive problems in dairy herds (Figure 1). Therefore, the introduction of bST into the United States does not explain the current rate of reproductive decline.

In addition to greater milk production and industry trends in herd management, a long list of other factors could partially explain deteriorating reproduction of US dairy cows. For example, inbreeding in US Holsteins has increased dramatically since 1980 (Figure 4; <http://www.aipl/arsusda.gov>) and may play a role in reproductive decline. Present levels of inbreeding are approximately 5% and some have predicted that levels of inbreeding will be 10% by 2020 (Hansen, 2000). Inbreeding negatively affects reproductive traits in dairy cows, but a “safe” level of inbreeding is poorly defined. In their analyses of Guernsey cattle, Hermas et al. (1987) concluded that every 1% increase in inbreeding led to a 0.17 increase in services per conception, a 2-d increase in days open, and a 3.3 percentage-unit decrease in conception rate. Their estimates had large standard errors but agreed with previous publications on inbreeding in dairy cows. If their estimates are correct, then the effects of inbreeding alone could account for

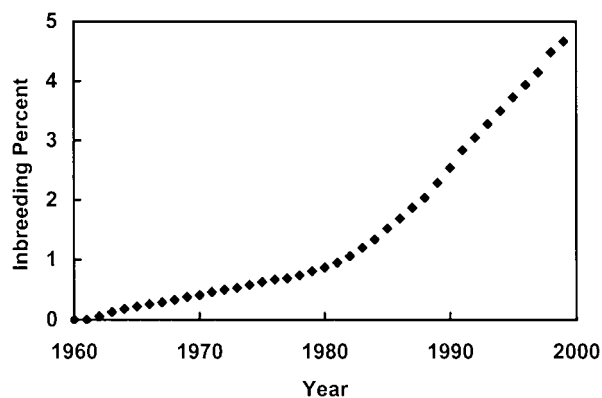


Figure 4. Average percentage inbreeding from 1960 to 1999 for US Holstein cows (USDA Animal Improvement Programs Laboratory; <http://aipl/arsusda.gov>).

an increase in days open of 7 d, an increase in services per conception of 0.6, and a decrease in conception rate of 12 percentage units since 1980.

One component of reproductive decline in dairy cattle may involve the changing global environment. The decade of the 1990s was the warmest since the beginning of instrumental temperature recording (Bradley, 2000). Reproduction in lactating dairy cows is extremely sensitive to heat stress because of the high metabolic rate associated with lactation (Wolfenson et al., 2000). Higher ambient temperatures will add to reproductive loss by causing heat stress in the summer and by expanding the regions within the United States where heat stress occurs. Al-Katanani et al. (1999) examined 90-d return rates throughout the calendar year and found that summer infertility was greatest in the highest milk producing dairy cattle. Therefore, there is an additive effect of heat stress and greater milk production for decreasing first-service conception rate in dairy cattle.

Finally, the decline in reproductive efficiency in dairy cattle may be arising from a completely unexpected source. Wild populations of frogs have declined worldwide since the 1970s, and there was an increased incidence of limb deformities in some populations (Morell, 1999). The effects of man-made endocrine-disrupting chemicals on developmental and reproductive processes (Crain and Guillet, 1998) presumably caused the die-offs and the deformed limbs. The effects of environmental toxins on development and reproduction in frogs, however, could never be recapitulated in laboratory tests. The frog die-offs and deformed limbs were later found to be caused by parasitic fungi (Morell, 1999) and flat worms (Johnson et al., 1999), respectively. Therefore, what seemed to be a logical cause for the decline in frog populations (environmental toxins) turned out to be a minor contributing factor to the phenomenon. Likewise, what we believe is causing reproductive decline in dairy cows (increased milk production, larger herds, etc.) could be having relatively minor effects compared with a larger undiscovered cause of infertility.

REPRODUCTIVE PHYSIOLOGY OF MODERN DAIRY COWS

Very few controlled studies have documented the changes in dairy reproductive physiology during the past 50 yr. Some universities initiated selection studies that were used to measure the effects of selection for milk production on reproductive physiology of dairy cows (Dunklee et al., 1994; Hageman et al., 1991; Hansen, 2000). Most of these studies were concluded before major declines in reproduction were experienced in US dairy cows. One selection project still in existence is

being conducted at the University of Minnesota (Hansen, 2000). Control and select lines were established in 1964 and have been continually selected since that time. The control line was maintained by using semen from 20 sires that were near the mean for PTA for milk yield in 1964. When the original semen supply was depleted, sons of cows and sires from the control line were selected and used to create a new supply of frozen semen. Select cows were mated to the four highest bulls for PTA for milk yield each year.

Reproductive change over time can also be estimated by retrospective studies of the scientific literature. Classical studies of dairy reproduction were completed in the 1950s and 1960s, and the literature means for reproductive values from this era can be compared with contemporary values. Although comparing studies across decades has obvious limitations, insights into long-term trends in reproduction can be gained.

Interval to First Ovulation

The interval to first ovulation in dairy cows has classically been described as occurring between 14 and 21 d after calving, with 5% of the herd anestrus at the start of the breeding season. The interval to first ovulation and percentage anestrus are based on studies completed before 1970 (Marion and Gier, 1968; Morrow et al., 1966). In modern dairy cows, the average interval to first ovulation is probably about 10 d longer, and the percentage of anestrus cows at the start of the breeding season may be considerably greater (Stevenson, 2000). Indeed, when we compared interval to first ovulation in the Minnesota cows, we found that the average interval to first ovulation was 29 ± 3 d and 43 ± 5 d for control (i.e., 1964) and select (i.e., modern) dairy cows, respectively. The corresponding percentages for anestrus cows (> 60 d postpartum) were 0 and 38%, respectively. Recent reports in the scientific literature confirm these trends for significantly longer intervals to first ovulation in postpartum dairy cows (deVries and Veerkamp, 2000; Lucy et al., 1992). Although the average interval to first ovulation is increasing, it is important to recognize that distributions for interval to first ovulation are skewed. In the deVries and Veerkamp (2000) study, the mean for interval to first ovulation was 29.7 d, but the mode was 18 d, an interval similar to that reported in the 1960s (Marion and Gier, 1968; Morrow et al., 1966). Therefore, the increase in the average interval to first ovulation in modern dairy cattle may be caused by a subpopulation of cows with extremely long intervals to first ovulation.

The reason for the delay in interval to first ovulation can be explained partially by greater negative energy balance in modern dairy cows. Lactating cows are gen-

erally in negative energy balance during the early postpartum period because they cannot consume adequate energy in the diet (Bauman and Currie, 1980). Negative energy balance reduces postpartum LH pulsatility and, therefore, delays the resumption of ovarian activity (Beam and Butler, 1999; Butler, 2000). Several investigators have documented the fact that negative energy balance causes a delay in interval to first ovulation and a delay in interval to first estrus. In their studies of 275 first-lactation heifers, however, deVries and Veerkamp (2000) found that only 3 to 4% of the variation in interval to first ovulation was explained by total energy deficit or energy balance nadir in early lactation. Furthermore, regression of the start of luteal activity on energy balance nadir had a slope near zero. Doubling the mean energy balance nadir for cows on the study would lengthen interval to first ovulation by only 4 d. In addition to negative energy balance, therefore, other factors are probably contributing to the increase in the interval to first ovulation in modern dairy cows.

The Estrous Cycle

Corpus luteum and progesterone. Progesterone is required for pregnancy in cattle. Pregnant cows have higher concentrations of blood progesterone within the first week to 10 d after insemination (Mann et al., 1999). Poor nutrition and weight loss in cattle causes a decrease in blood progesterone concentrations (Beal et al., 1978; Gombe and Hansel, 1973). One possibility is that greater milk production in dairy cattle is negatively affecting blood progesterone concentrations and causing infertility in dairy cows. We measured blood progesterone concentrations in the Minnesota study and found lower plasma concentrations of progesterone in select compared with control cows (Lucy et al., 1998). Therefore, based on data from the Minnesota selection study, a link between genetic selection for milk production and lower concentrations of blood progesterone was established.

There are several potential mechanisms for decreased progesterone in high-producing cows. Progesterone concentrations in blood are determined by rates of secretion, metabolism, and clearance of progesterone. Whether the size of the corpus luteum (CL) or progesterone secretion from the CL has changed in the past 50 yr is unknown. Few studies of CL weights in modern dairy cows in peak lactation have been completed. When we weighed CL from seven cows in peak lactation, we found an average CL weight of 3.7 g that was less than the average CL weight of New Zealand Friesian cows at a similar stage of lactation (5.1 g) (Bilby et al., 1998). The CL of high-producing dairy cows may be smaller, but the rates of progesterone secretion (per-

haps the more important measurement) have not been determined.

The size of the CL and secretion of progesterone is only part of the equation determining blood progesterone concentrations. Progesterone is cleared from blood through a variety of pathways. The liver is the primary site of progesterone metabolism, and progesterone and its metabolites are excreted in feces, urine, and milk (Parr, 1992). Rabiee et al. (2000) studied progesterone metabolism in dairy cows implanted with progesterone-releasing devices. They found that cows grazing pasture ad libitum had lower plasma concentrations of progesterone than cows grazing pasture for a restricted period of time (1.08 vs. 1.71 ng/ml for ad libitum versus restricted). Likewise, Sangsritavong et al. (2000) demonstrated that liver blood flow and progesterone metabolism increased by greater than 50% when feed intake was either acutely or chronically increased. Sheep were similar to cattle because progesterone metabolism increased with level of feeding (Parr, 1992). The conclusion from these studies is that modern dairy cows have lower blood concentrations of progesterone because they consume more feed and metabolize progesterone at a higher rate.

Progesterone is required for pregnancy, and there is an association between low progesterone and infertility. A direct link between low progesterone and embryonic loss has not, however, been established. Other factors associated with nutrition of the cow may affect the ovary and the pregnancy directly, but the two may not be related. For example, undernourished cows have smaller dominant follicles and smaller CL (Bossis et al., 1999), but their inability to become pregnant may be caused by a third mechanism that is unrelated to the changes that occur within the ovary. Finally, the absolute minimum blood progesterone concentrations that are needed for pregnancy in cattle are not known. Progesterone is transferred locally from the ovarian/oviductal venous drainage to the uterine artery in both sheep and cattle (Weems et al., 1988, 1989). The local transfer results in higher concentrations of progesterone within the uterus ipsilateral to the CL (Pope et al., 1982). Because of the local transfer, concentrations of progesterone in blood, which are the subject of rates of metabolism and clearance, may be irrelevant when progesterone is delivered to the uterus via the local circulation. Lozano et al. (1998) demonstrated this in sheep by showing that ewes fed a low-energy diet after ovulation had greater blood progesterone but lower uterine progesterone compared with ewes fed a high-energy diet after ovulation. Although local progesterone may be important for uterine function and pregnancy, changes in systemic progesterone may be affecting gonadotropin secretion that may ultimately change pat-

terns of follicular growth in modern dairy cows (see below).

In addition to lower progesterone, several groups have recently reported that modern dairy cows may have a higher proportion of abnormal luteal phases. Opsomer et al. (1998) examined postpartum luteal function in moderate-yielding Friesian dairy cows and high-yielding Holstein dairy cows. They found that the incidence of anestrus (delayed interval to first ovulation) was threefold higher in high-yielding cows (7 vs. 21%; Friesian vs. Holstein, respectively). In addition, Holstein cows were much more likely to have a prolonged luteal phase (high progesterone for greater than 20 d; 3 vs. 20%; Friesian versus Holstein, respectively). Lamming and Darwash (1998) found similar patterns of abnormal progesterone in UK cows. Likewise, we found that US Holsteins had longer luteal phases than New Zealand Friesian cows (Bilby et al., 1998), and cows in one study at the University of Missouri had average estrous cycle lengths of 24 to 28 d (Kirby et al., 1997). We did not detect differences in luteal phase length in select and control cows from the Minnesota herd (Lucy et al., 1998). Opsomer et al. (2000) performed an epidemiological study and concluded that negative energy balance, periparturient disorders, and postpartum diseases were risk factors for delayed cyclicity and prolonged luteal phases. Therefore, luteal phase abnormalities were linked to periparturient health and nutrition of dairy cattle.

A change in luteal phase length in modern-day dairy cows would complicate reproductive management. Longer luteal phases delay breeding in cows that are not in controlled breeding programs and make it more difficult to predict when cyclic cows will return to estrus. Although we have not specifically studied prolonged luteal phases in postpartum cows, we have observed prolonged luteal phases in heat-stressed cows and heifers (Wilson et al., 1998a, 1998b). In those studies, heat stress decreased plasma concentrations of estradiol and delayed the time of luteolysis by 9 d in lactating cows. Follicular estradiol is a critical component of the luteolytic cascade (Silvia et al., 1991). We concluded from our heat-stress work, therefore, that the prolonged luteal phases in heat-stress cattle were caused by inadequate estradiol secretion from a follicle that was presumably damaged by heat stress. The long luteal phases in modern dairy cows may reflect poor follicular health, reduced estradiol secretion, enhanced estradiol metabolism, and the failure of the luteolytic cascade through a follicular estradiol-dependent mechanism.

Follicular growth and estradiol. As mentioned above, postpartum dairy cows undergo a natural process of nutrient partitioning, negative energy balance, and weight loss during the early postpartum period

(Bauman and Currie, 1980). Negative energy balance and weight loss have an inhibitory effect on ovarian follicular growth and development. The mechanisms through which negative energy balance inhibits follicular development are complex and recently have been reviewed by several authors (Beam and Butler, 1999; Butler, 2000; Roche et al., 2000; Royal et al., 2000). Two potential mediators of the effects of negative energy balance on the follicle are LH and IGF-I (Lucy, 2000). Pulses of LH are decreased in cows in negative energy balance. Plasma concentrations of IGF-I also are decreased in the same cows. Luteinizing hormone and IGF-I act synergistically to promote follicular development (Lucy, 2000). The combined effect of a reduction in both hormones is, therefore, believed to compromise follicular growth in cows during the early postpartum period.

Beam (1995) studied the effects of negative energy balance on follicular growth in early postpartum cows. He observed that the dominant follicle in cows in negative energy balance required more time and a larger size to establish blood estradiol concentrations capable of triggering ovulation. Thus, follicles in negative energy balance cows may be less estrogenic and may achieve greater estrogenic capacity at a larger size. Peripheral estradiol metabolism also may be greater during negative energy balance so that a higher level of estrogen synthesis may be necessary to achieve equivalent blood estradiol concentrations. Data from Beam (1995) agree with a recent report that compared the estrous cycle of lactating cows and heifers (Sartori et al., 2000). Lactating cows had larger preovulatory follicles than did heifers but lower preovulatory concentrations of estradiol in blood. Whether lower blood estradiol concentrations in lactating cows are a consequence of lower steroidogenic capacity of the follicle or enhanced estrogen metabolism is not known.

Oocytes from large persistent follicles are less fertile than oocytes from smaller growing follicles (Austin et al., 1999). The additional time and size required for ovulation in lactating cows may be creating a follicle with characteristics of a persistent follicle. Persistent follicles are exposed to high concentrations of LH and oocytes are prematurely activated (Revah and Butler, 1996). The possibility that premature activation or aging of the oocyte before ovulation is causing infertility in dairy cows needs to be addressed in future studies.

Dairy cows are classified as monoovulatory and monotocous species. Modern dairy cows, however, have an ovulation rate of approximately 1.25 and a twinning rate of approximately 5% (Fricke and Wiltbank, 1999). Twinning is undesirable because milk production and fertility after a twin birth are decreased (Beerepoot et al., 1992). Kinsel et al. (1998) performed an epidemio-

logical study of twinning in dairy cows and found that twinning increased from 1.4 to 2.4% from 1983 to 1992. Furthermore, high milk production was a risk factor for twinning. Although enhanced embryonic survival may play a role, the greater percentage of twin births is most likely caused by a greater incidence of multiple ovulations in high-producing dairy cows (Fricke and Wiltbank, 1999). Indeed, Sartori et al. (2000) found that 25% of lactating cows experienced multiple ovulation during an estrous cycle. Their data agreed with our studies in which we found multiple ovulations in approximately 20% of lactating cows (Kirby et al., 1997). Sartori et al. (2000) also reported that the incidence of multiple ovulation in heifers was 2%, and this low rate of multiple ovulation agrees conceptually with the fact that twinning is rare in first-lactation cows (Kinsel et al., 1998).

The recent increase in twinning (presumably caused by higher ovulation rates) may represent a manifestation of poor follicular function and inadequate estradiol signaling in modern dairy cows (Fricke and Wiltbank, 1999). Cows undergo waves of follicular development that are synchronized by increases in plasma FSH (Roche et al., 1999). Estradiol and inhibins are essential for controlling follicular growth through their inhibitory effects on FSH during the follicular wave. The decrease in blood estradiol concentrations in lactating cows theoretically reduces negative feedback on FSH during a follicular wave. Follicular growth, therefore, may be increased in lactating cows through an increase in FSH. The possibility that other mechanisms controlling follicular growth (inhibins or undiscovered factors) are compromised by lactation also exists.

Estrus Expression

Detection of estrus is an essential component of postpartum breeding programs that depend on overt signs of estrus for optimal timing of insemination. The current decline in reproductive efficiency in dairy cows could be associated with poor estrus expression. Dransfield et al. (1998) performed an exhaustive analysis of data generated from electronic mount detectors (Heat-Watch System, DDx Inc., Denver, CO). The average dairy cow had 8.5 stands per estrus with an estrous duration of 7 h. Nearly one-quarter of the cows had estruses that were classified as low intensity (<1.5 stands/h) and short duration (<7 h). Therefore, detection of estrus is difficult in dairy cows if observation periods occur only twice daily for less than 30 min. Longer, more frequent observation periods may be necessary to accurately detect estrus in modern dairy cows. In addition to failure to detect estrus, the misidentification of estrus is also a problem in today's herds. In

a recent study of a research herd of 242 Holsteins, Sturman et al. (2000) found that 19% of inseminations were performed on cows in the luteal phase or early phases of pregnancy. Inseminations of pregnant cows led to 17% embryonic loss.

Few studies have systematically evaluated the causes of poor estrus expression in dairy cows. Estrus expression is hard to study because estrus is a behavior that originates from the actions of estradiol on the hypothalamus (Allrich, 1994). The intensity (number of mounts) and the duration of estrus depends on behavior of individual cows as well as social interactions among cows. Therefore, estrous intensity and duration must be examined in large studies before conclusions can be made. Britt et al. (1986) studied ovariectomized cows treated with estradiol and concluded that milk yield did not influence the intensity of estrus expression. Their original study, however, demonstrated the importance of surface because duration of estrus, mounting activity, and standing activity were greater on dirt than on concrete. Vailes and Britt (1990) confirmed the original observations of Britt et al. (1986) and showed that mounting activity was 15-fold greater on a dirt floor than on a concrete floor. If a decrease in estrus expression is occurring in modern dairy cows, then the most likely cause is the increased utilization of dairy confinement housing with concrete floors.

Ovarian Disease

Cystic ovary is present in approximately 10% of US dairy cows (Garverick, 1997). Increased milk production is a risk factor for cystic ovary (Heuer et al., 1999), and cystic ovary is a risk factor for infertility in dairy cows (Table 2). Therefore, the incidence of cystic ovary and infertility associated with cystic ovary will increase with future increases in milk production.

Pregnancy

Oocyte and sperm health. Pregnancy begins at conception (union of egg and sperm), but factors affecting the health of the gametes may ultimately determine the developmental competence of the embryo. Britt (1994) proposed the theory that the developmental competence of the oocyte is determined during the long period of follicular growth that precedes ovulation. Thus, diseases and disorders may negatively affect oocytes within follicles that begin their development during the early postpartum period. Heat stress is an example of these "carryover" effects on fertility. Cows have decreased conception in the summer and do not achieve normal fertility until the late fall, long after heat stress has ended (Wolfenson et al., 2000).

Table 3. Effect of genetic merit for milk yield, milk yield, BCS, and parity on the in vitro formation of blastocysts from fertilized oocytes (Snijders et al., 2000).

Classification of oocyte donor cow	Percent blastocyst formation (n)
Genetic merit for milk yield*	
High	6.8 (23/338)
Low	11.4 (41/359)
120-d milk yield (kg)	
3162 to 3972	9.9 (18/181)
4559 to 5114	10.1 (13/129)
BCS*	
1.5 to 2.5	3.0 (4/134)
3.3 to 4.0	9.9 (15/152)
Parity*	
First lactation	3.9 (5/130)
Third lactation	10.4 (59/567)

* $P < 0.05$.

Oocytes collected from dairy cows subjected to heat stress have reduced developmental competence in vitro (Rocha et al., 1998). However, whether the oocyte is affected by periparturient health and energy balance is still unclear. Gwazdauskas et al. (2000) collected oocytes throughout lactation by twice weekly follicular aspiration and concluded that stage of lactation and dietary energy influenced oocyte quality. They also reported lower success rates for lactating compared with nonlactating cows. Snijders et al. (2000) found that the ability of an oocyte to be fertilized and develop to the blastocyst stage in vitro was not affected by the milk production of the donor cow. Body condition, however, influenced oocyte competence because in vitro fertilized oocytes from cows in low body condition had a lower cleavage rate and a lower developmental rate compared with oocytes from cows in better body condition (Table 3). They also noted reduced developmental competence of oocytes collected from high genetic merit and first-lactation cows, again suggesting that reproductive efficiency is compromised by genetic selection as well as first lactation (see above).

Dairy reproductive physiologists tend to focus on the cow and ignore the importance of the bull for successful reproduction. We assume that the fertility of sires used for AI has not declined over the past 50 yr and that reproductive decline is arising from female infertility during lactation. Loss of sire fertility seems unlikely because conception rates for virgin heifers bred by AI have not markedly changed during the period of declining cow fertility (Butler and Smith, 1989). Nevertheless, summaries of reproductive statistics of virgin heifers have not been published recently and would be a valuable tool for assessing changes in reproduction that occur independently of lactation. Furthermore, the sensitivity of dairy cows to changes in semen quality may

be greater than for heifers that are not facing the additional demands of lactation.

Early embryonic development. Infertility in dairy cattle is not a new phenomenon, but the current trends in reproduction are different because reproductive problems affect a large percentage of dairy cows. The classical literature defined a class of dairy cattle known as “repeat breeders”; cows that were inseminated multiple times (usually four or more) and did not become pregnant. In his classic paper on repeat breeders, Casida (1961) had an even more stringent attitude toward the topic of “repeat breeders:”

“This reviewer sees no good reason, however, if semen quality and insemination circumstances are optimal, for the animal not qualifying as a repeat breeder upon a single return from service.” (L.E. Casida)

Even if we use less stringent criteria (four or more inseminations), many dairy cows in today’s herds could be classified as repeat breeders. Studies of repeat breeders showed that the repeat breeders were different from normal cows because there was a high rate of embryonic death (Ayalon, 1978). Embryonic death occurred at two different stages, both early (shortly after conception) and late (at the filamentous stage). Filamentous stage embryos were smaller in repeat breeder cows and may have been incapable of blocking the luteolytic cascade. The presence of smaller embryos suggests that the uterus was incapable of supporting normal embryonic development or that the embryos were defective. When reciprocal embryo transfer was done between repeat breeder and normal cattle, the repeat breeder cattle failed to achieve normal pregnancy rates even though an embryo from a “normal” cow was implanted (Gustafsson and Larsson, 1985). Conversely, normal cattle had normal rates of pregnancy when implanted with an embryo from a repeat breeder cow. These data suggest that repeat breeders and perhaps modern dairy cows fail to establish pregnancy because of a suboptimal uterine environment.

We do not know why embryos fail to develop within the uterus of otherwise normal cows. The uterus may fail to synthesize adequate amounts of an embryotrophic growth factor that is required by filamentous embryos. Secretion of embryotrophic growth factors into the uterine lumen may be controlled by nutritional status because embryo transfer pregnancy rates are less in recipients with low BCS (Mapletoft et al., 1986). Insulin-like growth factors and IGF binding proteins are nutritionally regulated and may have important roles in the process (Watson et al., 1999). The bovine embryo contains receptors for IGF-I, and IGF-I mRNA

is found in the uterus (Robinson et al., 2000). Furthermore, pregnant cows have higher concentrations of uterine IGF-I mRNA than nonpregnant cows (Kirby et al., 1996). Moreira et al. (2000) treated cows with bST after insemination and increased conception rates perhaps through an embryotrophic mechanism involving IGF-I. Likewise, Bilby et al. (1999) demonstrated a 5% increase in conception when beef and dairy cows were treated with bST at the time of insemination.

Even in normal cattle, there are high rates of embryonic loss between the period of conception and maternal recognition of pregnancy (about 17 to 19 d after insemination) (Mann et al., 1999). Losses after this early period are considerably less but nevertheless influence pregnancy rates. Classical studies of embryonic mortality in dairy cows estimated that approximately 10% of embryos were lost between 28 and 75 d of pregnancy (Kummerfeld et al., 1978). Embryonic loss during this period was much higher for repeat breeder cows (Ayalon, 1978; Casida, 1961). More recent studies employing ultrasonographic pregnancy detection suggest that the rate of embryonic loss between 28 and 60 d is at least 20% (Vasconcelos et al., 1997; Pursley et al., 1998) (Figure 5). It is impossible to compare historical data on embryonic loss with the recent estimates because most of the recent estimates are based on ultrasound technology that was not routinely used in cattle before the 1980s. Furthermore, most studies of embryonic mortality in modern dairy cows have involved cows subjected to a timed AI protocol. Rates of embryonic loss for modern cows inseminated at a spontaneous estrus may be lower. For example, Smith and Stevenson (1995) reported an embryonic loss rate of 12.4% after d 28 in cows that were inseminated at a spontaneous estrus.

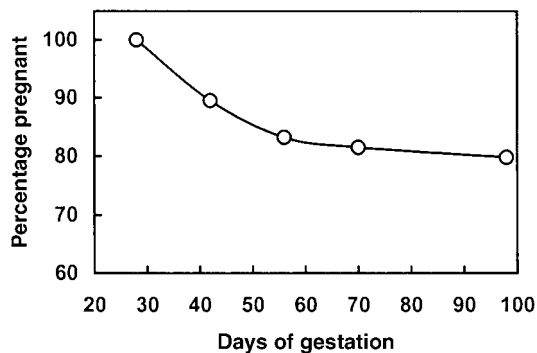


Figure 5. Percentage pregnancy from d 28 to 98 of gestation for lactating dairy cows inseminated by using a timed AI protocol and initially diagnosed pregnant by ultrasound on d 28 of gestation (Vasconcelos et al., 1997).

IMPORTANT AREAS FOR FUTURE RESEARCH

Applied Reproductive Management

The reproduction of lactating dairy cows should be managed by using either biweekly injections of $\text{PGF}_{2\alpha}$, followed by estrus detection or by using a timed AI protocol. The use of $\text{PGF}_{2\alpha}$ and estrus detection is good but suffers from the age-old problem of detecting cows in estrus. Combining regular $\text{PGF}_{2\alpha}$ injections with some type of estrus detection aid (e.g., patches and electronic devices) improves the overall response but requires additional management and attention to details. If cows are inseminated at spontaneous estrus, then the timing of insemination is critical (Dransfield et al., 1998; Nebel et al., 2000; Sacke et al., 2000). The old recommendation of twice-daily estrus detection for 30 min and insemination by the a.m.-p.m. rule needs to be modified. Estrus detection should be done more often for longer periods and cows should be inseminated 6 to 8 h after first observation of estrus. Electronic devices that are mounted on the tailhead may be the best way to insure accuracy in estrus detection. In any case, cows housed exclusively on concrete will have less-intense estrus and will be more difficult to detect when in estrus (Vailes and Britt, 1990).

Timed AI for insemination of dairy cattle represents an important change in reproductive management because cows are inseminated without estrus detection. Inseminating cows at a predetermined time is not a new concept because it was tried in the 1970s and 1980s (Lucy et al., 1986; Roche, 1977). The discovery that a follicular wave could be synchronized to improve the consistency of the follicular development around $\text{PGF}_{2\alpha}$ injection was, however, an important step forward because it improved the responses to timed AI and enabled the widespread implementation of the method (Twagiramungu et al., 1995). Timed AI is a good approach, but rates of embryonic loss after timed AI are high, and calving rates for dairy cows after timed AI are approximately 35%. These percentages are slightly better than those obtained in the 1970s and 1980s but are less than percentages for cows inseminated after a spontaneous estrus (approximately 45%) (Nebel and Jobst, 1998). Therefore, methods for timed insemination of dairy cattle still need to be optimized. Optimization may involve various types of synchronization before timed AI or may require a completely new approach for synchronizing follicular development, estrus, and ovulation.

Timed insemination and regular $\text{PGF}_{2\alpha}$ injections are good ways to control the time of first insemination. Only 20 to 50% of dairy cows will, however, be pregnant after first insemination. The fate of the 50 to 80% of dairy cows that are open after first insemination usually de-

depends on detecting the return to estrus after the pregnancy fails. The timing of second estrus after insemination is variable because many cows have an embryo that dies around the time of maternal recognition of pregnancy. Although the embryo is nonviable, it nevertheless can delay the luteolytic mechanisms and cause a variable delay in estrus (Van Cleeff et al., 1996). The fact that inseminated cows represent a mixture of pregnant and nonpregnant cows and that nonpregnant cows have a variable return to estrus complicates methods that can be used to synchronize second service. A hormonal approach involving a progesterone insert, estradiol benzoate injection, and PGF_{2 α} injection was developed in Australia for the purpose of synchronizing three inseminations in a 56-d period [J. Cavalieri and K. L. Macmillan (2000), unpublished]. Similar methods need to be developed for US dairy cows.

The dairy industry has very few tools for the pharmacological control of the estrous cycle, and new methods and new tools for estrous cycle control are desperately needed. Most of the drugs used to synchronize estrus were developed 30 to 50 yr ago, at a time when other areas of biology were in their infancy. Progesterone was first used to synchronize estrus in heifers in 1948 by Christian and Casida (1948). Their work was done 5 yr before the discovery of DNA (Watson and Crick, 1953). Whereas the biotechnology revolution has occurred since that time, the limitations of progesterone for synchronizing estrus have not been fully resolved. For example, Christian and Casida (1948) noted the importance of dosage and the potential for the development of cystic (persistent?) follicles. These two concerns are still present when progesterone or progestogens are used today. Likewise, the inability of PGF_{2 α} to cause luteolysis in the early phase of the estrous cycle has not been overcome (Lauderdale, 1972). Clearly, renewed emphasis is needed to solve the limitations of these traditional drugs and to develop completely new classes of drugs that synchronize estrus and ovulation in new and different ways.

New procedures for reproductive management and pharmacological control of the estrous cycle need to be tied to computerized management systems capable of making decisions ("smart" computers). The reproductive management of a large herd of lactating dairy cows cannot be efficiently managed with a pencil and a notebook. This is particularly true if economic decision-making is incorporated into the breeding program (DeLorenzo et al., 1992). The tools and technology are available to let computers decide whether a cow should be scheduled for rebreeding (based on her production) and when to do it (based on the economics of the farm and the individual lactation curve of the cow). If timed AI is used, then the programming becomes simpler be-

cause inseminations can be scheduled. If electronic methods of heat detection are used (pedometers or mount detectors), then the computer needs to be able to integrate the information with whatever else is known about the cow (e.g., previous estrous dates, treatments, and changes in milk production) and make decisions on the likelihood of estrus. In either case, the system needs to be linked to automatic sort gates so that the decision the computer makes can be enacted. Farm workers can then implement the management (e.g., injections, inseminations, and pregnancy check) on the sorted pen of cows and feed data back into the system.

Metabolic Effects of Lactation on Reproduction

The focus of reproductive physiologists has been the high-producing dairy cow, but cows with moderate milk production also have reproductive problems. Therefore, there are general effects of lactation on reproduction in dairy cows. Virgin heifers have high first-service conception rates; the assumption is that parturition and subsequent lactation lead to an appreciably lower conception rate. The inherently negative effects of parturition and lactation on reproduction may not, however, be great. Lactating beef cattle may suffer from anestrus, but once they are cycling, their conception rates are approximately 20 percentage points higher than dairy cattle (Stevenson et al., 2000). Likewise, New Zealand dairy cows, whose milk production is low compared with US standards, have high first-service conception rates (Macmillan et al., 1996). There may be a minimum milk production after which reproductive efficiency declines, and this minimum may not be reached by either beef cattle or New Zealand dairy cattle. Australian, Irish, and UK dairy cattle may now, however, have reached the minimum and are now experiencing reproductive decline. US dairy cattle probably reached the minimum several decades ago.

The metabolic and endocrine signals that cause lower conception rates in dairy cows need to be defined. Many candidates have been tested in the past, and we understand a lot more about the endocrine cues that control reproductive function than we once did (Beam and Butler, 1999; Butler, 2000; Roche et al., 2000; Royal et al., 2000). Pulsatility of LH secretion is clearly important to the resumption of estrous cyclicity, and rapid progress has been made in understanding the hypothalamic factors that control GnRH and thus LH. Other metabolic hormones like insulin and IGF-I may act synergistically with LH to promote follicular development in postpartum cows (Lucy, 2000). A host of other hormones and metabolites might be involved (Rabiee et al., 1999). Before great strides in the area of lactational effects on reproduction can be made, however, the basic nutri-

tional and hormonal requirements of the granulosa cell, the theca cell, and the oocyte must be understood. Once that is known, then the constraints that lactation places on these cells will be clearer.

Mechanisms Linking Disease to Infertility in Postpartum Cows

Epidemiological studies of reproduction in dairy cattle consistently demonstrate the negative effects of disease on fertility of postpartum cows. Progress toward understanding the mechanisms behind the effects of disease on reproduction has been slow in the past. The slow progress can probably be traced back to the separation of the large animal veterinary community from the large animal research community. Veterinarians who understand disease and the treatment of disease may not be interested in applying the scientific method to their therapies. At the same time, animal scientists (with Ph.D.s) who are interested in applying the scientific method are not trained in disease or the treatment of disease. These two communities (veterinarians and Ph.D. scientists) must be brought together in meaningful collaborations so that the basic mechanisms linking postpartum disease to infertility in dairy cattle can be identified.

Early Embryonic Death

Perhaps the most surprising component of reproductive loss in dairy cattle is the large number of seemingly normal embryos that undergo early embryonic death. Rates of embryonic loss are high in "normal" cows and may be even higher in cows whose insemination is poorly timed with ovulation and cows that are inseminated by timed AI. To my knowledge, there is no inherent biological requirement for a high rate of embryonic loss in dairy cows with genetically normal embryos. Understanding embryonic loss in dairy cows may reveal ways to alleviate early embryonic loss. Correcting embryonic loss and achieving extremely high rates of conception in dairy cattle (>90%) would completely change the way we manage the lactation cycle. Instead of inseminating a cow at random postpartum intervals, dairymen could inseminate once at the most profitable postpartum interval for the individual cow.

STRATEGIES FOR IMPROVING DAIRY REPRODUCTION

The problems facing reproduction in dairy cattle are not simple. A reversal in the current trends can be achieved only through a variety of approaches. Selection of cows for improved reproductive efficiency is one

possibility. Reproductive traits have low heritabilities, but the coefficient of variation of reproductive traits is very large (Philipsson, 1981). Therefore, genetic selection for improved daughter fertility is possible in dairy cattle. The problem is that there are negative genetic correlations between daughter fertility and milk yield. Scandinavian breeding programs include functional nonproduction traits (e.g, fertility and mastitis resistance) in addition to production traits in their selection indices for total merit (Philipsson et al., 1994). Although progress toward greater milk production may be less, their models suggest better economic efficiency when functional nonproduction traits are included in selection programs (Philipsson et al., 1994).

There is clearly a need to get back to basics in terms of the reproductive management of lactating cows. Reproduction is a complex process, and successful herd reproduction requires meticulous attention to detail. Periparturient health, uterine and ovarian health, estrus detection, time of insemination relative to estrus, semen handling, AI technique, and pregnancy diagnosis are as important today as they were 50 yr ago. Minor mistakes in these procedures have cumulative effects on herd reproduction. Pre- and postpartum nutrition (including protein nutrition; Butler, 2000) have a large effect on reproductive efficiency. Therefore, feed analyses and ration balancing are essential. Education and retraining with an emphasis on large herds probably can correct part of the reproductive decline in the dairy industry if those in charge of herd reproduction are given incentives to do better.

Declining reproduction will not be solved completely through education, however, because we still do not understand a lot about reproduction in lactating dairy cattle. In addition, new methods for managing reproduction must be developed. To make progress in the present research environment, the dairy science research community must expand the number of investigators, coordinate its activities across investigators, and build infrastructure for research. Talented new investigators need to be attracted to dairy science research by offering large multi-year research grants. The grants must include training programs for new graduate students and include incentives for young investigators. Investigators interested in key areas such as the interaction of reproduction and nutrition and early embryonic death should also be targeted.

Solving the problem in dairy reproduction will require additional dollars for research and extension. Unfortunately, federal funding for agricultural research has not kept pace with the demand for new knowledge. The primary source for competitive grant funding for agricultural research outside the USDA Agricultural Research Service is the USDA National Research Ini-

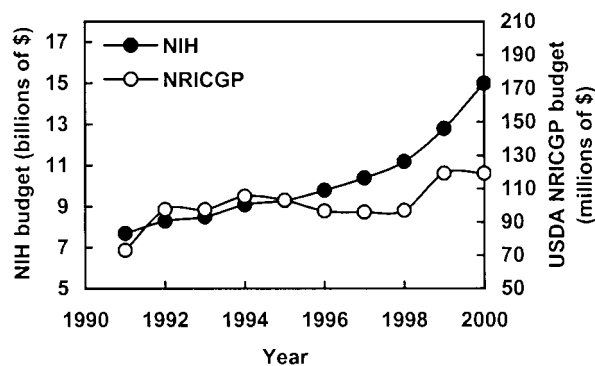


Figure 6. Federal extramural grant funding from 1991 to 2000 for the USDA National Research Initiative Competitive Grants Program (NRICGP) and the National Institutes of Health (NIH).

tiative Competitive Grants Program (**NRICGP**). The USDA NRICGP was started in 1991, with a budget of only about one-hundredth the amount of extramurally funded grants of the National Institutes of Health (**NIH**). Since that time, the total funding for the USDA NRI has changed little, whereas NIH funding has increased steadily (Figure 6). The current funding for agricultural research must be increased immediately if agricultural research is to remain viable in the public sector. Even with an immediate infusion of research dollars, it will take decades to rebuild an agricultural research community that has been hurt by a lack of consistent federal funding.

Finally, new information and technology needs to be transferred rapidly back to the agricultural community. This is the only way to guarantee continued support from state and federal governments for agricultural research. The InCalf project of the Australian Dairy Research and Development Corporation is a good example of a project conducted at a national level that fed information directly back to producers. After the data were analyzed, booklets that discussed the results were prepared and distributed to farmers and veterinarians across Australia. The booklets contained information that was useful to farmers (Table 1). Because of this feedback, most Australian farmers are aware of the InCalf project and support the work that has been done.

CONCLUSIONS

Reproductive efficiency in dairy cows is decreasing worldwide. The increase in milk production per cow is one factor contributing to the problem. In addition to milk production, however, many other equally important factors may be involved. These factors include increasing herd size, greater use of confinement housing, labor shortages, higher inbreeding percentages,

and global warming. In response to genetic selection for milk production, the reproductive physiology of dairy cattle also has changed. Compared with traditional dairy cows, modern dairy cows have longer intervals to first ovulation, a higher incidence of anestrus and abnormal luteal phases, lower blood progesterone and IGF-I concentrations, higher multiple ovulation and twinning rates, and greater embryonic loss. Reproductive decline can be reversed in dairy cows, but a collective effort within the dairy community (e.g., farmers, veterinarians, researchers, and extension agents) will be necessary before great strides can be made.

ACKNOWLEDGMENTS

The author expresses his sincere appreciation to the ADSA Foundation for their generous support of young investigators through the ADSA Foundation Scholar Award.

REFERENCES

- al-Katanani, Y. M., D. W. Webb, and P. J. Hansen. 1999. Factors affecting seasonal variation in 90-day nonreturn rate to first service in lactating Holstein cows in a hot climate. *J. Dairy Sci.* 82:2611–2616.
- Allrich, R. D. 1994. Endocrine and neural control of estrus in dairy cows. *J. Dairy Sci.* 77:2738–2744.
- Austin, E. J., M. Mihm, M. P. Ryan, D. H. Williams, and J. F. Roche. 1999. Effect of duration of dominance of the ovulatory follicle on onset of estrus and fertility in heifers. *J. Anim. Sci.* 77:2219–2226.
- Ayalon, N. 1978. A review of embryonic mortality in cattle. *J. Reprod. Fertil.* 54:483–493.
- Bauman, D. E., and W. B. Currie. 1980. Partitioning of nutrients during pregnancy and lactation: a review of mechanisms involving homeostasis and homeorhesis. *J. Dairy Sci.* 63:1514–1529.
- Bauman, D. E. 1999. Bovine somatotropin and lactation: from basic science to commercial application. *Domest. Anim. Endocrinol.* 17:101–116.
- Bauman, D. E., R. W. Everett, W. H. Weiland, and R. J. Collier. 1999. Production responses to bovine somatotropin in northeast dairy herds. *J. Dairy Sci.* 82:2564–2573.
- Beal, W. E., R. E. Short, R. B. Staigmiller, R. A. Bellows, C. C. Kaltenbach, and T. G. Dunn. 1978. Influence of dietary energy intake on bovine pituitary and luteal function. *J. Anim. Sci.* 46:181–188.
- Beam, S. W. 1995. Follicular Development in Postpartum Cattle: Effects of Energy Balance and Dietary Lipid. Ph.D. Dissertation, Cornell University, Ithaca, NY.
- Beam, S. W., and W. R. Butler. 1999. Effects of energy balance on follicular development and first ovulation in postpartum dairy cows. *J. Reprod. Fertil. Suppl.* 54:411–424.
- Beerepoot, G. M., A. A. Dykhuizen, M. Nielen, and Y. H. Schukken. 1992. The economics of naturally occurring twinning in dairy cattle. *J. Dairy Sci.* 75:1044–1051.
- Bilby, C. R., K. L. Macmillan, G. A. Verkerk, J. A. Peterson, A. T. Koenigsfeld, and M. C. Lucy. 1998. A comparative study of ovarian function in American (US) and New Zealand (NZ) Friesian lactating dairy cows. *J. Anim. Sci.* 76(Suppl. 1):222. (Abstr.)
- Bilby, C. R., J. F. Bader, B. E. Salfen, R. S. Youngquist, C. N. Murphy, H. A. Garverick, B. A. Crooker, and M. C. Lucy. 1999. Plasma GH, IGF-I, and conception rate in cattle treated with low doses of recombinant bovine GH. *Theriogenology* 51:1285–1296.
- Bossis, I., R. P. Wettemann, S. D. Welty, J. A. Vizcarra, L. J. Spicer, and M. G. Diskin. 1999. Nutritionally induced anovulation in beef

- heifers: ovarian and endocrine function preceding cessation of ovulation. *J. Anim. Sci.* 77:1536–1546.
- Bradley, R. 2000. 1000 years of climate change. *Science* 288:1353–1355.
- Britt, J. H. 1994. Follicular development and fertility: potential impacts of negative energy balance. Pages 103–112 in the Proc. Natl. Reprod. Symp., Pittsburgh, PA.
- Britt, J. H., R. G. Scott, J. D. Armstrong, and M. D. Whitacre. 1986. Determinants of estrous behavior in lactating Holstein cows. *J. Dairy Sci.* 69:2195–2202.
- Butler, W. R. 1998. Review: effect of protein nutrition on ovarian and uterine physiology in dairy cattle. *J. Dairy Sci.* 81:2533–2539.
- Butler, W. R. 2000. Nutritional interactions with reproductive performance in dairy cattle. *Anim. Reprod. Sci.* 60–61:449–457.
- Butler, W. R., and R. D. Smith. 1989. Interrelationships between energy balance and postpartum reproductive function in dairy cattle. *J. Dairy Sci.* 72:767–783.
- Casida, L. E. 1961. Present status of the repeat-breeder cow problem. *J. Dairy Sci.* 44:2323–2329.
- Christian, R. E., and L. E. Casida. 1948. The effects of progesterone in altering the estrous cycle of the cow. *J. Anim. Sci.* 7:540. (Abstr.)
- Cole, W. J., K. S. Madsen, R. L. Hintz, and R. J. Collier. 1991. Effect of recombinantly-derived bovine somatotropin on reproductive performance of dairy cattle. *Theriogenology* 36:573–595.
- Collier, R. J., J. C. Byatt, T. Curran, P. J. Eppard, A. C. Fabellar, R. L. Hintz, R. Hoffman, M. M. McCrate, C. L. McLaughlin, R. H. Sorbet, and J. L. Vicini. 1997. Post-approval evaluation of POSILAC bovine somatotropin in 28 commercial dairy herds. *J. Dairy Sci.* 80(Suppl. 1):169. (Abstr.)
- Crain, D. A., and L. J. Guillette, Jr. 1998. Reptiles as models of contaminant-induced endocrine disruption. *Anim. Reprod. Sci.* 53:77–86.
- de Vries, M. J., and R. F. Veerkamp. 2000. Energy balance of dairy cattle in relation to milk production variables and fertility. *J. Dairy Sci.* 83:62–69.
- DeLorenzo, M. A., T. H. Spreen, G. R. Bryan, D. K. Beede, and J. A. Van Arendonk. 1992. Optimizing model: insemination, replacement, seasonal production, and cash flow. *J. Dairy Sci.* 75:885–896.
- Dematawewa, C. M., and P. J. Berger. 1998. Genetic and phenotypic parameters for 305-day yield, fertility, and survival in Holsteins. *J. Dairy Sci.* 81:2700–2709.
- Dransfield, M. B., R. L. Nebel, R. E. Pearson, and L. D. Warnick. 1998. Timing of insemination for dairy cows identified in estrus by a radiotelemetric estrus detection system. *J. Dairy Sci.* 81:1874–1882.
- Dunklee, J. S., A. E. Freeman, and D. H. Kelley. 1994. Comparison of Holsteins selected for high and average milk production. 2. Health and reproductive response to selection for milk. *J. Dairy Sci.* 77:3683–3690.
- Emanuelson, U., and P. A. Oltenacu. 1998. Incidences and effects of diseases on the performance of Swedish dairy herds stratified by production. *J. Dairy Sci.* 81:2376–2382.
- Fricke, P. M., and M. C. Wiltbank. 1999. Effect of milk production on the incidence of double ovulation in dairy cows. *Theriogenology* 52:1133–1143.
- Garverick, H. A. 1997. Ovarian follicular cysts in dairy cows. *J. Dairy Sci.* 80:995–1004.
- Goldberg, J. J., E. E. Wildman, J. W. Pankey, J. R. Kunkel, D. B. Howard, and B. M. Murphy. 1992. The influence of intensively managed rotational grazing, traditional continuous grazing, and confinement housing on bulk tank milk quality and udder health. *J. Dairy Sci.* 75:96–104.
- Gombe, S., and W. Hansel. 1973. Plasma luteinizing hormone (LH) and progesterone levels in heifers on restricted energy intakes. *J. Anim. Sci.* 37:728–733.
- Gröhn, Y. T., and P. J. Rajala-Schultz. 2000. Epidemiology of reproductive performance in dairy cows. *Anim. Reprod. Sci.* 60–61:605–614.
- Gustafsson, H., and K. Larsson. 1985. Embryonic mortality in heifers after artificial insemination and embryo transfer: differences between virgin and repeat breeder heifers. *Res. Vet. Sci.* 39:271–274.
- Gwazdauskas, F. C., K. W. Kendrick, A. W. Pryor, and T. L. Bailey. 2000. Impact of follicular aspiration on folliculogenesis as influenced by dietary energy and stage of lactation. *J. Dairy Sci.* 83:1625–1634.
- Hageman, W.H.D., G. E. Shook, and W. J. Tyler. 1991. Reproductive performance in genetic lines selected for high or average milk yield. *J. Dairy Sci.* 74:4366–4376.
- Hansen, L. B. 2000. Consequences of selection for milk yield from a geneticist's viewpoint. *J. Dairy Sci.* 83:1145–1150.
- Hermas, S. A., C. W. Young, and J. W. Rust. 1987. Effects of mild inbreeding on productive and reproductive performance of Guernsey cattle. *J. Dairy Sci.* 70:712–715.
- Heur, C., Y. H. Schukken, and P. Dobbelaar. 1999. Postpartum body condition score and results from the first test day milk as predictors of disease, fertility, yield, and culling in commercial dairy herds. *J. Dairy Sci.* 82:295–304.
- Johnson, P. T., K. B. Lunde, E. G. Ritchie, and A. E. Launer. 1999. The effect of trematode infection on amphibian limb development and survivorship. *Science* 284:802–804.
- Kaneene, J. B., and R. Miller. 1994. Epidemiological study of metritis in Michigan dairy cattle. *Vet. Res.* 25:253–257.
- Kinsel, M. L., W. E. Marsh, P. L. Ruegg, and W. G. Etherington. 1998. Risk factors for twinning in dairy cows. *J. Dairy Sci.* 81:989–993.
- Kirby, C. J., W. W. Thatcher, R. J. Collier, F. A. Simmen, and M. C. Lucy. 1996. Effects of growth hormone and pregnancy on expression of growth hormone receptor, insulin-like growth factor-I, and insulin-like growth factor binding protein-2 and -3 genes in bovine uterus, ovary, and oviduct. *Biol. Reprod.* 55:996–1002.
- Kirby, C. J., M. F. Smith, D. H. Keisler, and M. C. Lucy. 1997. Follicular function in lactating dairy cows treated with sustained-release bovine somatotropin. *J. Dairy Sci.* 80:273–285.
- Kummerfeld, H. L., E. A. Oltenacu, and R. H. Foote. 1978. Embryonic mortality in dairy cows estimated by nonreturns to service, estrus, and cyclic milk progesterone patterns. *J. Dairy Sci.* 61:1773–1777.
- Lamming, G. E., and A. O. Darwash. 1998. The use of milk progesterone profiles to characterize components of subfertility in milked dairy cows. *Anim. Reprod. Sci.* 52:175–190.
- Lauderdale, J. W. 1972. Effects of PGF₂ α on pregnancy and estrous cycle of cattle. *J. Anim. Sci.* 35:246. (Abstr.)
- Loeffler, S. H., M. J. de Vries, and Y. H. Schukken. 1999a. The effects of time of disease occurrence, milk yield, and body condition on fertility of dairy cows. *J. Dairy Sci.* 82:2589–2604.
- Loeffler, S. H., M. J. de Vries, Y. H. Schukken, A. C. de Zeeuw, A. A. Dijkhuizen, F. M. de Graaf, and A. Brand. 1999b. Use of AI technician scores for body condition, uterine tone and uterine discharge in a model with disease and milk production parameters to predict pregnancy risk at first AI in Holstein dairy cows. *Theriogenology* 51:1267–1284.
- Lozano, J. M., J. A. Abecia, F. Forcada, L. Zarazaga, and B. Alfaro. 1998. Effect of undernutrition on the distribution of progesterone in the uterus of ewes during the luteal phase of the estrous cycle. *Theriogenology* 49:539–546.
- Lucy, M. C. 2000. Regulation of ovarian follicular growth by somatotropin and insulin-like growth factors in cattle. *J. Dairy Sci.* 83:1635–1647.
- Lucy, M. C., J. S. Stevenson, and E. P. Call. 1986. Controlling first service and calving interval by prostaglandin F₂ α , gonadotropin-releasing hormone, and timed insemination. *J. Dairy Sci.* 69:2186–2194.
- Lucy, M. C., C. R. Staples, W. W. Thatcher, P. S. Erickson, R. M. Cleale, J. L. Firkins, M. R. Murphy, J. H. Clark, and B. O. Brodie. 1992. Influence of diet composition, dry matter intake, milk production, and energy balance on time of postpartum ovulation and fertility in dairy cows. *Anim. Prod.* 54:323–331.
- Lucy, M. C., W. J. Weber, L. H. Baumgard, B. S. Seguin, A. T. Koenigsfeld, L. B. Hansen, H. Chester-Jones, and B. A. Crooker. 1998. Reproductive endocrinology of lactating dairy cows selected for increased milk production. *J. Anim. Sci.* 76(Suppl. 1):296. (Abstr.)
- Macmillan, K. L., I. J. Lean, and C. T. Westwood. 1996. The effects of lactation on the fertility of dairy cows. *Aust. Vet. J.* 73:141–147.
- Mann, G. E., G. E. Lamming, R. S. Robinson, and D. C. Wathes. 1999. The regulation of interferon-tau production and uterine

- hormone receptors during early pregnancy. *J. Reprod. Fertil. Suppl.* 54:317–328.
- Mapletoft, R. J., C. E. Lindsell, and V. Pawlshyn. 1986. Effects of clenbuterol, body condition, and nonsurgical embryo transfer equipment on pregnancy rates in bovine recipients. *Theriogenology* 25:172. (Abstr.)
- Marion, G. B., and H. T. Gier. 1968. Factors affecting bovine ovarian activity after parturition. *J. Anim. Sci.* 27:1621–1626.
- Moreira, F., C. A. Risco, M. F. Pires, J. D. Ambrose, M. Drost, and W. W. Thatcher. 2000. Use of bovine somatotropin in lactating dairy cows receiving timed artificial insemination. *J. Dairy Sci.* 83:1237–1247.
- Morell, V. 1999. Are pathogens felling frogs? *Science* 284:728–731.
- Morrow, D. A., S. J. Roberts, K. McEntee, and H. G. Gray. 1966. Postpartum ovarian activity and uterine involution in dairy cattle. *J. Am. Vet. Med. Assoc.* 149:1596–1609.
- Nebel, R. L., and S. M. Jobst. 1998. Evaluation of systematic breeding programs for lactating dairy cows: a review. *J. Dairy Sci.* 81:1169–1174.
- Nebel, R. L., and M. L. McGilliard. 1993. Interactions of high milk yield and reproductive performance in dairy cows. *J. Dairy Sci.* 76:3257–3268.
- Nebel, R. L., M. G. Dransfield, S. M. Jobst, and J. H. Bame. 2000. Automated electronic systems for the detection of oestrus and timing of AI in cattle. *Anim. Reprod. Sci.* 60–61:713–723.
- O'Farrell, K. J., and J. Crilly. 1999. Trends in first service calving rates in Irish dairy herds 1991–1996, Page 52 in *Proceedings of Fertility in the High-Producing Dairy Cow. Occasional Meeting of the British Society of Animal Science*, Galway, Ireland.
- Opsomer, G., M. Coryn, H. Deluyker, and A. de Kruif. 1998. An analysis of ovarian dysfunction in high yielding dairy cows after calving based on progesterone profiles. *Reprod. Domest. Anim.* 33:193–204.
- Opsomer, G., Y. T. Grohn, J. Hertl, M. Coryn, H. Deluyker, and A. de Kruif. 2000. Risk factors for post partum ovarian dysfunction in high producing dairy cows in Belgium: a field study. *Theriogenology* 53:841–857.
- Parr, R. A. 1992. Nutrition-progesterone interactions during early pregnancy in sheep. *Reprod. Fertil. Dev.* 4:297–300.
- Philipsson, J. 1981. Genetic aspects of female fertility in dairy cattle. *Livest. Prod. Sci.* 8:307–319.
- Philipsson, J., G. Banos, and T. Arnason. 1994. Present and future uses of selection index methodology in dairy cattle. *J. Dairy Sci.* 77:3252–3261.
- Pope, W. F., R. R. Maurer, and F. Stormshak. 1982. Distribution of progesterone in the uterus, broad ligament, and uterine arteries of beef cows. *Anat. Rec.* 203:245–250.
- Pursley, J. R., M. R. Kosorok, and M. C. Wiltbank. 1997a. Reproductive management of lactating dairy cows using synchronization of ovulation. *J. Dairy Sci.* 80:301–306.
- Pursley, J. R., M. C. Wiltbank, J. S. Stevenson, J. S. Ottobre, H. A. Garverick, and L. L. Anderson. 1997b. Pregnancy rates per artificial insemination for cows and heifers inseminated at a synchronized ovulation or synchronized estrus. *J. Dairy Sci.* 80:295–300.
- Pursley, J. R., R. W. Silcox, and M. C. Wiltbank. 1998. Effect of time of artificial insemination on pregnancy rates, calving rates, pregnancy loss, and gender ratio after synchronization of ovulation in lactating dairy cows. *J. Dairy Sci.* 81:2139–2144.
- Rabiee, A. R., I. J. Lean, J. M. Gooden, and B. G. Miller. 1999. Relationships among metabolites influencing ovarian function in the dairy cow. *J. Dairy Sci.* 82:39–44.
- Rabiee, A. R., K. L. Macmillan, and F. Schwarzenberger. 2000. Effect of level of feed intake on plasma progesterone concentrations in deslorelin-implanted dairy cows treated with a CIDR device. *J. Anim. Sci.* 78(Suppl. 1):221. (Abstr.)
- Revah, I., and W. R. Butler. 1996. Prolonged dominance of follicles and reduced viability of bovine oocytes. *J. Reprod. Fertil.* 106:39–47.
- Risco, C. A., G. A. Donovan, and J. Hernandez. 1999. Clinical mastitis associated with abortion in dairy cows. *J. Dairy Sci.* 82:1684–1689.
- Robinson, R. S., G. E. Mann, T. S. Gadd, G. E. Lamming, and D. C. Wathes. 2000. The expression of the IGF system in the bovine uterus throughout the oestrous cycle and early pregnancy. *J. Endocrinol.* 165:231–243.
- Rocha, A., R. D. Randel, J. R. Broussard, J. M. Lim, R. M. Blair, J. D. Roussel, R. A. Godke, and W. Hansel. 1998. High environmental temperature and humidity decrease oocyte quality in *Bos taurus* but not in *Bos indicus* cows. *Theriogenology* 49:657–665.
- Roche, J. F. 1977. Control of ovulation and fixed time insemination in heifers following cloprostenol. *Vet. Rec.* 100:468–470.
- Roche, J. F., E. J. Austin, M. Ryan, M. O'Rourke, M. Mihm, and M. G. Diskin. 1999. Regulation of follicle waves to maximize fertility in cattle. *J. Reprod. Fertil. Suppl.* 54:61–71.
- Roche, J. F., D. Mackey, and M. D. Diskin. 2000. Reproductive management of postpartum cows. *Anim. Reprod. Sci.* 60–61:703–712.
- Royal, M. D., A. O. Darwash, A.P.F. Flint, R. Webb, J. A. Woolliams, and G. E. Lamming. 2000. Declining fertility in dairy cattle: changes in traditional and endocrine parameters of fertility. *Anim. Sci.* 70:487–502.
- Saacke, R. G., J. C. Dalton, S. Nadir, R. L. Nebel, and J. H. Bame. 2000. Relationship of seminal traits and insemination time to fertilization rate and embryo quality. *Anim. Reprod. Sci.* 60–61:663–677.
- Sangsritavong, S., D. K. Combs, R. F. Sartori, and M. C. Wiltbank. 2000. Liver blood flow and steroid metabolism are increased by both acute feeding and hypertrophy of the digestive tract. *J. Anim. Sci.* 78(Suppl. 1):221. (Abstr.)
- Sartori, R. F., G. J. Haughian, M. Rosa, R. D. Shaver, and M. C. Wiltbank. 2000. Differences between lactating cows and nulliparous heifers in follicular dynamics, luteal growth, and serum steroid concentrations. *J. Anim. Sci.* 78(Suppl. 1):212. (Abstr.)
- Schmitt, E. J., T. Diaz, M. Drost, and W. W. Thatcher. 1996. Use of a gonadotropin-releasing hormone agonist or human chorionic gonadotropin for timed insemination in cattle. *J. Anim. Sci.* 74:1084–1091.
- Silvia, W. J. 1998. Changes in reproductive performance of Holstein dairy cows in Kentucky from 1972 to 1996. *J. Dairy Sci.* 81(Suppl. 1):244. (Abstr.)
- Silvia, W. J., G. S. Lewis, J. A. McCracken, W. W. Thatcher, and L. Wilson, Jr. 1991. Hormonal regulation of uterine secretion of prostaglandin F_{2α} during luteolysis in ruminants. *Biol. Reprod.* 45:655–663.
- Smith, M. W., and J. S. Stevenson. 1995. Fate of the dominant follicle, embryonal survival, and pregnancy rates in dairy cattle treated with prostaglandin F_{2α} and progestins in the absence or presence of a functional corpus luteum. *J. Anim. Sci.* 73:3743–3751.
- Snijders, S. E., P. Dillon, D. O'Callaghan, and M. P. Boland. 2000. Effect of genetic merit, milk yield, body condition and lactation number on in vitro oocyte development in dairy cows. *Theriogenology* 53:981–989.
- Stahl, T. J., B. J. Conlin, A. J. Seykora, and G. R. Steuernagel. 1999. Characteristics of Minnesota dairy farms that significantly increased milk production from 1989–1993. *J. Dairy Sci.* 82:45–51.
- Staples, C. R., W. W. Thatcher, and J. H. Clark. 1990. Relationship between ovarian activity and energy status during the early postpartum period of high producing dairy cows. *J. Dairy Sci.* 73:938–947.
- Stevenson, J. S. 1999. Can you have good reproduction and high milk yield? *Hoard's Dairyman* 144:536.
- Stevenson, J. S. 2000. Are your cows cycling; if not why? *Hoard's Dairyman* 145:202–203.
- Stevenson, J. S., K. E. Thompson, W. L. Forbes, G. C. Lamb, D. M. Grieger, and L. R. Corah. 2000. Synchronizing estrus and(or) ovulation in beef cows after combinations of GnRH, norgestomet, and prostaglandin F_{2α} with or without timed insemination. *J. Anim. Sci.* 78:1747–1758.
- Sturman, H., E. A. Oltenacu, and R. H. Foote. 2000. Importance of inseminating only cows in estrus. *Theriogenology* 53:1657–1667.
- Twagiramungu, H., L. A. Guilbault, and J. J. Dufour. 1995. Synchronization of ovarian follicular waves with a gonadotropin-releasing

- hormone agonist to increase the precision of estrus in cattle: a review. *J. Anim. Sci.* 73:3141–3151.
- Vailes, L. D., and J. H. Britt. 1990. Influence of footing surface on mounting and other sexual behaviors of estrual Holstein cows. *J. Anim. Sci.* 68:2333–2339.
- Van Cleeff, J., K. L. Macmillan, M. Drost, M. C. Lucy, and W. W. Thatcher. 1996. Effects of administering progesterone at selected intervals after insemination of synchronized heifers on pregnancy rates and resynchronization of returns to service. *Theriogenology* 46:1117–1130.
- Vasconcelos, J.L.M., R. W. Silcox, J. A. Lacerda, J. R. Pursley, and M. C. Wiltbank. 1997. Pregnancy rate, pregnancy loss, and response to heat stress after AI at 2 different times from ovulation in dairy cows. *Biol. Reprod.* 56(Suppl. 1):140. (Abstr.)
- Watson, A. J., M. E. Westhusin, and Q. A. Winger. 1999. IGF paracrine and autocrine interactions between conceptus and oviduct. *J. Reprod. Fertil. Suppl.* 54:303–315.
- Watson, J. D., and F.H.C. Crick. 1953. Molecular structure of nucleic acids. *Nature* 171:737.
- Weems, C. W., C. N. Lee, Y. S. Weems, and D. L. Vincent. 1988. Distribution of progesterone to the uterus and associated vasculature of cattle. *Endocrinol. Jpn.* 35:625–630.
- Weems, C. W., Y. S. Weems, C. N. Lee, and D. L. Vincent. 1989. Progesterone in uterine and arterial tissue and in jugular and uterine venous plasma of sheep. *Biol. Reprod.* 41:1–6.
- Wilson, S. J., C. J. Kirby, A. T. Koenigsfeld, D. H. Keisler, and M. C. Lucy. 1998a. Effects of controlled heat stress on ovarian function of dairy cattle. 2. Heifers. *J. Dairy Sci.* 81:2132–2138.
- Wilson, S. J., R. S. Marion, J. N. Spain, D. E. Spiers, D. H. Keisler, and M. C. Lucy. 1998b. Effects of controlled heat stress on ovarian function of dairy cattle. 1. Lactating cows. *J. Dairy Sci.* 81:2124–2131.
- Wolfenson, D., Z. Roth, and R. Meidan. 2000. Impaired reproduction in heat-stressed cattle: basic and applied aspects. *Anim. Reprod. Sci.* 60–61:535–547.