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Use it or lose it: Enhancing milk production efficiency by frequent milking of dairy cows[1]

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ABSTRACT: In the past century, great strides have been made toward optimizing milk production efficiency of dairy cows. One of the key findings that has emerged is that the milk yield of dairy cows is responsive to demands of offspring or milk removal; hence, milk production can be increased by frequent milking. Early studies illustrated the galactopoietic effect of frequent milking during the entire lactation, with 3 times daily milking increasing milk yield by up to 20% relative to twice daily milking. Later studies reported that cows produced more milk during the entire lactation if they were allowed to suckle a calf for the first 3 to 4 mo of lactation. The results of these experiments laid the groundwork for current research, which has identified a time during early lactation wherein the mammary gland of dairy cows is especially receptive to the stimulus of frequent milking. This window of time has from the first 10 wk of lactation to the first 6 wk, and it was subsequently established that frequent milking for a short duration within the first 3 wk of lactation can increase milk production through the remainder of lactation. In addition, there is strong evidence that this milk yield response is locally regulated. Consequently, the concept of "use it or lose it" is becoming more clearly established; that is, the stimulus of frequent milking during early lactation permanently increases the milk production capacity of the mammary gland. Exciting research opportunities now present themselves, and ongoing experiments seek to identify the local factors that are involved in the regulation of milk production efficiency of dairy cows.

Key words: frequent milking, mammary gland, milk production, suckling

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INTRODUCTION

Frequent milking (3 or more times daily) of dairy cows has emerged as an effective management tool for dairy farmers to increase milk production efficiency. Although it is a relatively novel management practice, the original interest and research in this area dates back to the late 1800s (Hills, 1890; Dean, 1898). Despite considerable variation in the magnitude of the milk yield response, it was recognized long ago that thrice-daily milking (**3X**) increased milk production relative to twice-daily milking (**2X**) and that frequent milking could be a profitable management tool if costs associated with the extra milkings are outweighed by the value of additional milk obtained (Riford, 1922; Dahlberg, 1924). Cows milked 3X generally produced about 20% more milk than those milked 2X, and milk production could be increased another 7% by milking 4 times daily (**4X**) instead of 3X (Woodward, 1931). Modern-day adjustment factors used to compare milk production of cows milked 2X to those milked 3X range from 12 to 14%, depending on the parity of the cow (VanRaden et al., 1999).

Since the establishment of the galactopoietic effect on milk production, several experiments have been conducted to identify the factors that regulate the milk yield response. These reports have documented consistent responses to increased milking frequency; however, questions remain about the mechanisms involved in regulation of milk production efficiency. The objectives of this review were to summarize the literature on frequent milking and to discuss the physiological bases and potential mechanisms involved in the response to frequent milking.

FREQUENT MILKING INCREASES MILK PRODUCTION

Much of the work on frequent milking for the entire lactation was conducted during the 1980s and 1990s, when there was great interest in switching milking re-

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Table 1. Summary of select literature reports on the effects of frequent milking (FM) on milk yield of dairy cows

Reference	Parity	Breed	Duration of FM	Change in milk yield (2X vs. 3X)[1]	Change in milk yield (2X vs. 4X)
Riford, 1922	≥1	Holstein; Guernsey	Unknown	+4.6 kg/d	
Woodward, 1931	≥1	Holstein	Full lactation	+20%	
Copeland, 1934	≥1	Jersey	Through late lactation	+21%	
Rao and Ludri, 1984	≥2	Brown Swiss × Sahiwal	50 to 130 DIM[2]	+1.34 kg/d	+1.73 kg/d
DePeters et al., 1985	≥2	Holstein	Full lactation	+17%	
	1	Holstein	Full lactation	+6% (NS)	
Amos et al., 1985	≥2	Holstein	Full lactation	+18.5%	
	1	Holstein	Full lactation	+25.2%	
Allen et al., 1986	≥2	Holstein	Full lactation	+13.4%	
	1	Holstein	Full lactation	+19.4%	
Gisi et al., 1986	≥2	Holstein	Full lactation	+12%	
	1	Holstein	Full lactation	+14%	
Barnes et al., 1990	1	Holstein	Full lactation	+14%	
Campos et al., 1994	1	Holstein	Full lactation	+17.3%	
	1	Jersey	Full lactation	+6.3%	
Klei et al., 1997	≥1	Holstein	Full lactation	+10.4%	
Smith et al., 2002	≥1	Holstein	Full lactation	+16%	

[1]Numbers in columns represent the increase in milk yield observed with increased milking frequency. 2X = twice-daily milking; 3X = thrice-daily milking; 4X = 4 times daily milking. NS = not significant.
[2]DIM = days in milk.

gimes from 2X to 3X to increase milk production efficiency (Table 1). Rao and Ludri (1984) reported that relative to 2X, 3X increased milk production by 1.34 kg/d and that 4X increased milk production by 1.73 kg/d compared with 3X. In summaries of Dairy Herd Improvement Association (DHIA) records, the increase in milk production with 3X was 12 to 16% compared with 2X (Allen et al., 1986; Gisi et al., 1986; Smith et al., 2002). These reports were obtained from mostly Holstein herds, or combined Holstein and Jersey herds. Culotta and Schmidt (1988) suggested that smaller dairy breeds do not respond as well to frequent milking as larger breeds. Consistent with that hypothesis were observations of Campos et al. (1994) that relative to 2X, 3X increased milk production by 17.3 and 6.3% in Holsteins and Jerseys, respectively. In contrast, Copeland (1934) observed an impressive 21 and 19% increase in milk and fat production, respectively, from Jerseys milked 3X compared with those milked 2X. In addition, they reported a correlation of 0.64 between the amount of milk cows produced before frequent milking and the magnitude of the response to frequent milking (Copeland, 1934). This led to speculation that greater-producing cows responded better to increased milking frequency than did lower-producing cows. The existence of such a relationship, however, has not been established. To the contrary, Erdman and Varner (1995) and Stockdale (2006) reviewed the literature on frequent milking and reported no correlation between previous milk production and the response to changes in milking frequency. Instead, those researchers concluded that there was an incremental milk yield response. Relative to 2X, this fixed milk yield response was –6.2, +3.5, and +4.9 kg/d for once-daily milking, 3X, or 4X, respectively (Erdman and Varner, 1995). In addition, this response is not specific to dairy cows; milk production was increased with frequent milking of other dairy ruminants, including goats (Wilde et al., 1986), sheep (Geenty and Davison, 1982; Negrao et al., 2001; Nudda et al., 2002), and buffalo (Dash et al., 1976).

Several research groups have characterized the economic gain observed with frequent milking. Factors contributing to the profitability of frequent milking were labor, herd size, herd health, management, feed costs, and milk price (Armstrong et al., 1985; Culotta and Schmidt, 1988; Maltz et al., 2003). Rao and Ludri (1984) reported that 3X increased net income by 21% relative to 2X. More recently, we estimated a net increase of approximately $93 per cow per year when cows were milked 4X for the first 3 wk of lactation and milked 2X thereafter (Wall and McFadden, 2007b). Therefore, assuming no negative effects on cow health or reproductive performance, frequent milking has the potential to be a very profitable management tool.

EFFECTS OF FREQUENT MILKING ON MILK COMPOSITION AND COW HEALTH

Reported effects of frequent milking on milk composition, somatic cell count (**SCC**), and herd health have been inconsistent. Many researchers have observed no effect of frequent milking on milk composition (Poole, 1982; Rao and Ludri, 1984; Amos et al., 1985; DePeters et al., 1985; Gisi et al., 1986), whereas some have observed a decrease in fat percentage (Allen et al., 1986; Smith et al., 2002). Due to the increase in milk production in response to frequent milking, however, there is often an increase in the total yield of fat and protein (Klei et al., 1997; Dahl et al., 2004b). With respect to SCC, some reports have indicated an association between frequent milking and decreased SCC, and these authors concluded that frequent milking may improve mammary health (Poole, 1982; Armstrong et al., 1985; Smith et al., 2002; Dahl et al., 2004b). Others have reported no effect of frequent milking on SCC (Waterman et al., 1983; DePeters et al., 1985; Gisi et al., 1986; Bar-Peled et al., 1995; Klei et al., 1997; Hale et al., 2003; Patton et al., 2006; Wall and McFadden, 2007a). The inconsistencies in the above reports may be the result of variations in timing and methods of sampling across experiments. Discrepancies also exist in the reported effects of frequent milking on reproductive performance and herd health. Some researchers have observed decreased reproductive performance in 3X cows compared with 2X cows (Ludwin, 1942; Armstrong et al., 1985; DePeters et al., 1985; Smith et al., 2002), whereas others have observed no effect (Poole, 1982; Amos et al., 1985; Gisi et al., 1986) or an improvement (Allen et al., 1986) in reproductive performance with 3X. Armstrong et al. (1985) suggested that any negative effects of frequent milking on herd health or reproductive performance may be associated with poor herd management. Well-controlled field studies using standardized sampling procedures will be necessary to verify the effect of milking frequency on milk composition, SCC, and herd health, and to identify the interaction between frequent milking and herd management on these factors.

EFFECT OF PARITY ON THE RESPONSE TO FREQUENT MILKING

It has been reported that the milk production response to frequent milking was more pronounced in animals with smaller udder capacity, such as heifers (Woodward, 1931; Copeland, 1934; Lush and Shrode, 1953). Copeland (1934) speculated that this may be a function of increased udder pressure associated with less udder capacity. In agreement with this, Allen et al. (1986) observed that relative to 2X, 3X increased milk production by 13.4 and 19.4% in cows and heifers, respectively. In the previous year, however, another group reported that mature cows respond better to frequent milking than primiparous cows (DePeters et al., 1985). Of the 5 studies represented in Table 1 that measured the milk yield response in heifers separately, 4 reported that heifers responded to frequent milking similarly to or better than multiparous cows. Therefore, no relationship has been established between parity and the magnitude of the milk yield response to frequent milking.

FREQUENT MILKING DURING EARLY LACTATION: A WINDOW OF OPPORTUNITY

An exciting development for both dairy producers and dairy scientists was the finding that the timing of implementation can influence the milk yield response to frequent milking. During middle and late lactation, frequent milking increased milk production; however, cessation of frequent milking resulted in an immediate decrease in milk yield to pretreatment levels (Elliott, 1961; Morag, 1973a,b; Svennersten et al., 1990). During early lactation, however, frequent milking for a short duration can stimulate milk production, and the effect persists through the remainder of lactation, even after less frequent milking is resumed. This effect was originally observed in experiments designed to determine the milk yield loss associated with the use of nurse cows. Using identical twin cows, Everitt and Phillips (1971) discovered that suckling by calves in addition to machine milking during the first 8 to 10 wk of lactation was associated with increased milk production after weaning and throughout the remainder of lactation in both primi- and multiparous cows. Shortly after this report, similar observations were made in both cows (Edmunds, 1977; Moss and O'Grady, 1978; Thomas et al., 1978; Fulkerson, 1981) and heifers (Fulkerson et al., 1978; Peel et al., 1979). A similar effect of frequent milking during early lactation on milk yield is illustrated by comparison of panels A and B in Figure 1. Figure 1, panel A, shows the lactation curves of cows milked 2X or 3X for the entire lactation (redrawn from Amos et al., 1985). Three-times daily milking increased milk production both at peak and through the entire lactation. Persistency of the lactation curve was also slightly increased, but this effect disappeared after approximately 180 d in milk (**DIM**; Figure 1, panel A). Pearson et al. (1979) observed almost an identical milk yield response to Amos et al. (1985). They assigned cows to 3X for the first 143 d of lactation, followed by 2X thereafter (Figure 1, panel B). Although they did not report the full lactation curves, they measured milk yield for the entire lactation and reported that relative to 2X, cows that were milked 3X for the first 143 d of lactation produced more milk through 280 DIM (Pearson et al., 1979). Subsequently, it has been observed in numerous experiments that frequent milking during early lactation was associated with both acute and persistent increases in milk production (Table 2). These findings presented an opportunity for dairy producers that an initial investment in labor could increase milk production efficiency for the remainder of lactation. Poole (1982) speculated that the practice might not be adopted, however, because producers would be discouraged by the partial decrease in milk production upon cessation of frequent milking, despite the significant carryover effect.

In an attempt to minimize additional costs associated with frequent milking, and to investigate the response of dairy cows to frequent milking or suckling during a short interval of time in early lactation, Bar-Peled et al. (1995) compared 3X to 6 times daily milking (**6X**) or 3X plus suckling for the first 6 wk of lactation, followed by 3X of all cows. Relative to cows milked 3X during the entire lactation, 6X and 3X plus suckling acutely increased milk production by 7.3 and 14.7 kg/d, respectively (Bar-Peled et al., 1995). Cessation of frequent milking or suckling was associated with a partial decline in milk production; however, a carryover effect was observed in 6X cows (+5.1 kg/d relative to 3X; Bar-Peled

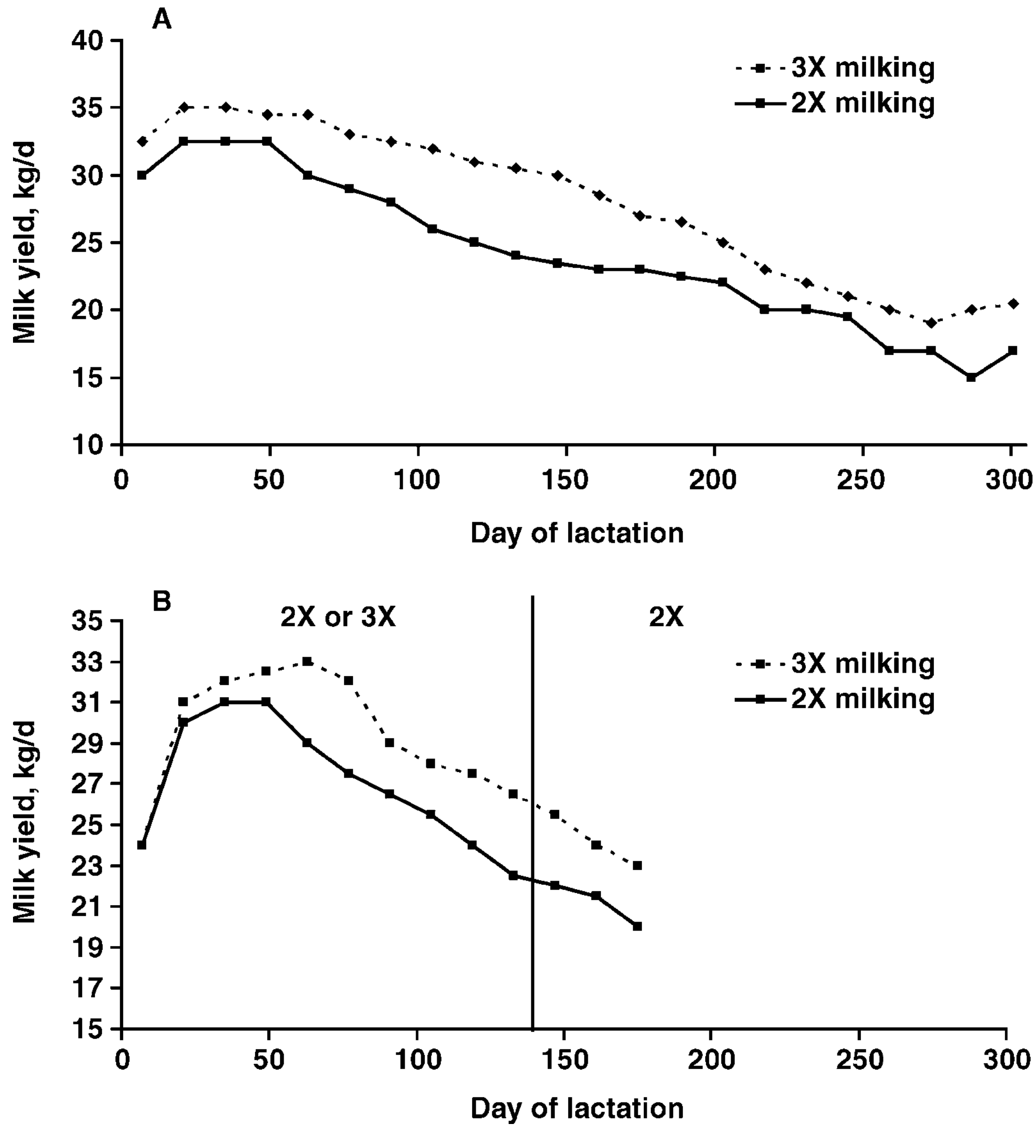

Figure 1. Panel A. Lactation curves of multiparous cows milked twice (2X) or thrice (3X) daily for the entire lactation (redrawn from Amos et al., 1985; used by permission from the Journal of Dairy Science; 68:732–739). Panel B. Lactation curves of multiparous cows milked 2X or 3X for the first 143 d of lactation followed by 2X for the remainder of lactation; the vertical line indicates the cessation of frequent milking (redrawn from Pearson et al., 1979; used by permission from the Journal of Dairy Science; 62:1941–1950).

et al., 1995). In a similar experiment, Sanders et al. (2000) observed an acute increase of 6 kg/d and a carryover response of 3.7 kg/d in 6X cows relative to 3X cows. In heifers, the acute response to 6X was lower in magnitude (+1.7 kg/d), and no carryover effect was observed (Sanders et al., 2000).

The results of subsequent experiments have further narrowed down the window during early lactation wherein frequent milking can increase milk production for the remainder of lactation. Hale et al. (2003) assigned cows to 2X or to 4X for the first 3 wk of lactation, followed by 2X. Four-times-daily milking was associated with an acute increase of 8.8 kg/d and a carryover effect of 2.6 kg/d for the remainder of lactation. A treatment interval of 1 to 21 DIM was also used in a field study by Dahl et al. (2004b), who observed similar effects of frequent milking during early lactation. In contrast, VanBaale et al. (2005) assigned cows to 3X or 6X for the first 7, 14, or 21 d of lactation and reported that 6X did not increase milk production relative to 3X. Their observations were inconsistent with previous reports, and the authors speculated that facility logistics may have influenced their results, because 6X cows were housed farther away from the milking parlor and spent a considerably longer time away from their pen than 3X cows (VanBaale et al., 2005). With the exception of the recent negative report (VanBaale et al., 2005), and a recent abstract (Fernandez et al., 2004), it is generally accepted that frequent milking increases milk yield and that frequent milking during early lactation can increase milk production for the

Table 2. Summary of select literature reports on the effects of frequent milking during early lactation on milk yield of dairy cows[1]

Reference	Treatment duration, DIM[1]	Parity	Change in milk yield (2X vs. 1X + suckle),[2] %	Change in milk yield (2X vs. 2X + suckle), kg/d	Change in milk yield (2X vs. 3X), kg/d	Change in milk yield (2X vs. 4X), kg/d	Change in milk yield (3X vs. 6X), kg/d
Everitt and Phillips, 1971	1 to 70	≥2		+1.2 (pers.[3])			
		1		0.87 (pers.)			
Moss and O'Grady, 1978	1 to 56	≥2		+3.3			
				No. pers.			
Thomas et al., 1978	1 to 56	≥2		+1.68 (acute[4])			
				+1.77 (pers.)			
Fulkerson et al., 1978	1 to 56	1	+16 (full lactation)				
Pearson et al., 1979	1 to 150	≥2			+2.2 (full lactation)		
Peel et al., 1979	1 to 28	1	+13 (pers.)				
Fulkerson et al., 1981	1 to 7	≥2	+9 (pers.)				
Poole, 1982	1 to 140	≥2			+4.4 (acute)		
					+1.84 (pers.)		
		1			+2.17 (acute)		
					+0.65 (pers.)		
Bar-Peled et al., 1995	1 to 42	≥2					+7.3 (acute)
							+5.1 (pers.)
Sanders, 2000	1 to 42	≥2					+6.0 (acute)
							+3.7 (pers.)
		1					+1.7 (acute)
							No pers.
Hale et al., 2003	1 to 21	≥2				+8.6 (acute)	
						+2.6 (pers.)	
Dahl et al., 2004b	1 to 21	≥2					+14 (acute)
							+3.7 (full lactation)
VanBaale et al., 2005	1 to 7	≥2					−1.7 (acute)
	1 to 14	≥2					+0.2 (acute)
	1 to 14	≥2					−2.3 (acute)
							No pers.

[1]DIM = days in milk.
[2]Numbers in columns represent the increase in milk yield observed with increased milking frequency. 1X = once-daily milking; 2X = twice-daily milking; 3X = thrice-daily milking; 4X = 4 times daily milking; 6X = 6 times daily milking.
[3]Pers. = the persistent increase in milk production after cessation of frequent milking or suckling.
[4]Acute = the increase in milk production during frequent milking or suckling.

remainder of lactation (see Tables 1 and 2). The mechanistic basis for the milk yield response to frequent milking, however, is poorly understood. Even less understood are the mechanisms involved in the persistent effect on milk yield of frequent milking during early lactation.

LOCAL REGULATION OF MILK PRODUCTION

There is substantial evidence in support of local regulation of milk production within the gland, independent of systemic factors (Wilde et al., 1995). Knight et al. (1998) and Delamaire and Guinard-Flament (2006) concluded that the increase in pressure during long milking intervals resulted in the breakdown of tight junctions and loss of epithelial function. However, when mammary pressure was maintained during frequent milking by replacement with a sucrose solution into the mammary gland, milk production was not affected (Henderson and Peaker, 1984). An alternate hypothesis was that there existed a chemical in milk that negatively regulated milk secretion between milkings (Linzell and Peaker, 1971). A small glycoprotein in milk, named feedback inhibitor of lactation (**FIL**), has been shown to reversibly inhibit casein and lactose synthesis, and it has been suggested that FIL may be involved in autocrine regulation of milk secretion (Wilde et al., 1995). Surprisingly, however, work on FIL has dwindled since the 1990s, and there have been no recent reports to confirm the role of this protein in the bovine mammary gland.

UNILATERAL FREQUENT MILKING

Shortly after the report in the 1930s that frequent milking increased milk production, several studies utilized unilateral frequent milking (**UFM**) to investigate the effect. Half-udder designs are extremely powerful, because they eliminate variation among animals due to environment, nutrition, and genetics. In addition, both udder halves are theoretically exposed to the same systemic factors; hence, responses to frequent milking are strictly at the level of the mammary gland. A summary of the milk yield response to frequent milking in selected half-udder experiments is presented in Table 3. The

Table 3. Summary of select literature reports on the effects of unilateral frequent milking (UFM) on milk yield[1]

Reference	Species	Stage of lactation	Duration of UFM	Parity	Change in milk yield (1X vs. 2X),[1] kg/d	Change in milk yield (2X vs. 3X), %	Change in milk yield (2X vs. 4X)
Ludwick et al., 1941	Cow	Unknown	35 d	≥2		+16	
Cash and Yapp, 1950	Cow		Full lactation	≥2		+32	
Agarwala and Sundaresan, 1955	Cow	Early	25-d intervals	≥2		+8.4	
Elliott, 1961	Cow	Mid	39 d	≥1		+12	
Morag, 1968	Sheep	Early	8-d intervals	≥2	−0.15	ND	
Morag, 1973a	Cow	Peak	11-d intervals	≥2		+11	
Hillerton et al., 1990	Cow	Mid-late	28 d	≥1			+10.4%
Knight et al., 1992	Cow	Mid	14 d	1			+14%
Knight, 1992	Goat	Early	42 d	≥1		+10.4	
Nudda et al., 2002	Sheep	Mid	4-d intervals	≥1	−0.15		
Boutinaud et al., 2003	Goat	Late	23 d	?		+8	
Norgaard et al., 2005	Cow	Mid	7 d	≥1			+18%
Wall and McFadden, 2007a	Cow	1 DIM[2]	21 d	≥2			+3.5 kg/d (acute[3]) +1.8 kg/d (pers.[4])
Wall and McFadden, 2007b	Cow	1 DIM	14 d	≥2			+3.7 kg/d (acute) +1.2 kg/d (pers.)
	Cow	7 DIM	14 d	≥2			+2.9 kg/d (acute) +1.5 kg/d (pers.)

[1]Numbers in columns represent the increase in milk yield observed with increased milking frequency. 1X = once-daily milking; 2X = twice-daily milking; 3X = thrice-daily milking; 4X = 4 times daily milking.
[2]DIM = days in milk.
[3]Acute = the increase in milk production during frequent milking.
[4]Pers. = the persistent increase in milk production after frequent milking.

early reports provided strong evidence for local regulation of milk production, and increases in milk yield from 8.4 to 32% in the frequently milked udder half were observed (Ludwick et al., 1941; Cash and Yapp, 1950; Agarwala and Sundaresan, 1955; Claesson et al., 1959). Morag (1973a) reported that the increase in milk production in response to UFM occurs within 24 h, and the magnitude of the response was independent of previous milk production. In addition, heifers respond to UFM; Hillerton et al. (1990) milked udder halves 2X or 4X for 4 wk during midlactation. In both cows and heifers, milk production of 4X udder halves increased by 10.4% relative to 2X udder halves (Hillerton et al., 1990).

As mentioned previously, an emerging theme in these experiments has been that the effects of frequent milking during early lactation on milk production persist even after a lower milking frequency is resumed (Bar-Peled et al., 1995; Hale et al., 2003; Dahl et al., 2004b). Although this persistent milk yield response has been consistently observed (Table 2), it was unknown whether the response was regulated by hormones, by local factors within the mammary gland, or by the combination of the two. To investigate this question, we used a half-udder model and assigned cows to UFM (4X of the right udder half, 2X of the left udder half) for d 1 to 21 of lactation, followed by 2X for the remainder of lactation (Wall and McFadden, 2007a). When the half-udder milk yields were adjusted to the equivalent of a whole-udder basis, the acute and long-term milk yield responses to frequent milking that we observed were consistent with those reported by Hale et al. (2003). Therefore, our results indicated that both the acute and persistent effects of frequent milking during early lactation are regulated by local factors within the mammary gland. This is illustrated in Figure 2, panels A and B. Figure 2, panel A (redrawn from Bar-Peled et al., 1995), shows the milk yield response of multiparous cows to 6X for the first 6 wk of lactation, followed by 3X. We observed a similar effect using a half-udder experiment (Figure 2, panel B), and the milk yield response lasted through 270 DIM. This finding presents some intriguing questions and research opportunities. First, what are the local factors that regulate milk production capacity of the mammary gland? Once the factors have been identified and pathways understood, how can we refine our approach to maximize milk production efficiency of dairy cows? Now that it is established that the factors are indeed local, the problem has become relatively simplified. Extremely powerful, within-cow experiments that are less sensitive to the influence of environment, genetics, and nutrition can now be designed to ask such mechanistic questions.

On the road to refinement, one theme that has transpired is the existence of a window of time wherein the mammary gland is especially responsive to frequent

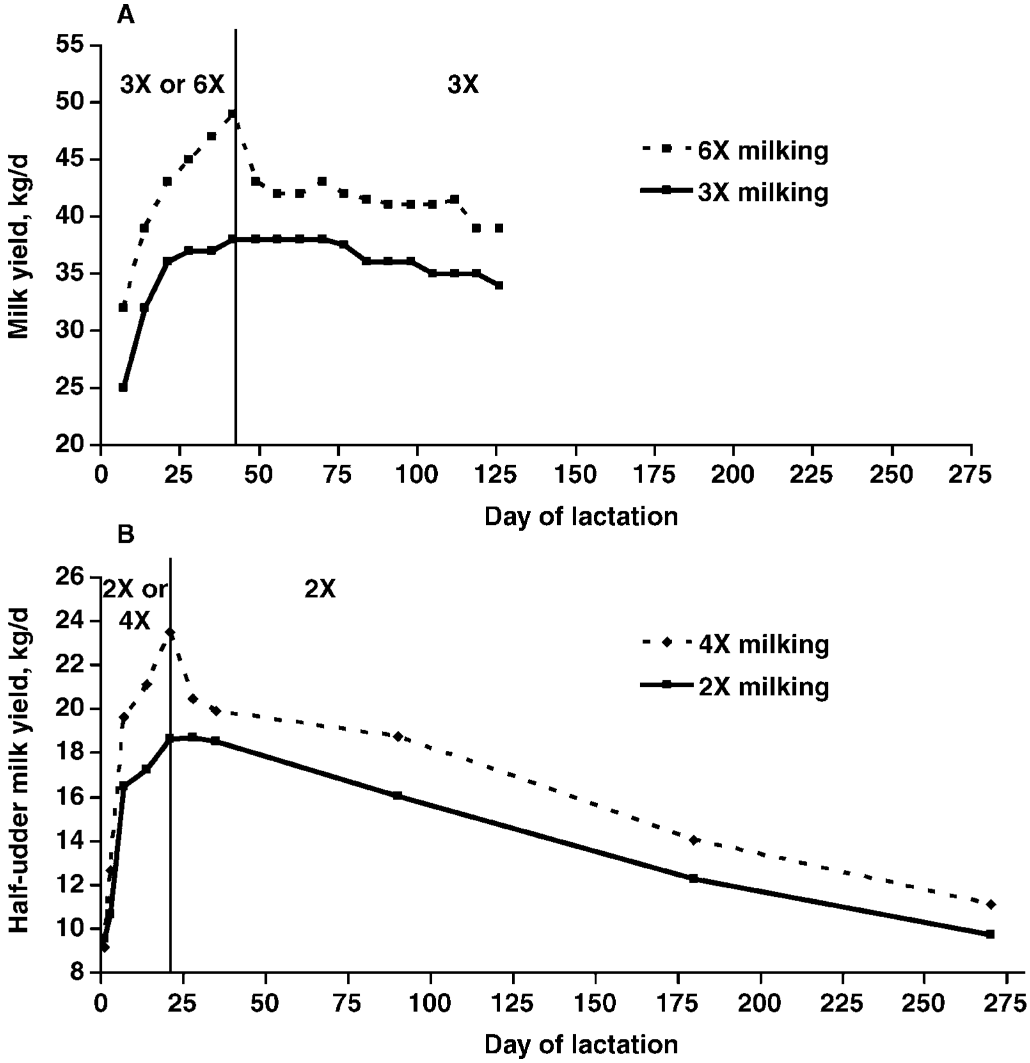

Figure 2. Panel A. Lactation curves of multiparous cows milked six times daily (6X) for d 1 to 42 of lactation or thrice daily (3X) for the entire lactation (redrawn from Bar-Peled et al., 1995; used by permission from the Journal of Dairy Science; 78:2726–2736). Panel B. Lactation curves of multiparous cows milked 4 times daily (4X) unilaterally for d 1 to 21 or twice daily for the entire lactation (2X; from E. H. Wall and T. B. McFadden, unpublished results). Vertical lines indicate cessation of frequent milking.

milking. The duration of this window has been shortened from the first 10 wk of lactation (Moss and O'Grady, 1978; Thomas et al., 1978) to the first 6 wk of lactation (Bar-Peled et al., 1995; Sanders et al., 2000) and shortened further still to the first 3 wk of lactation (Hale et al., 2003; Dahl et al., 2004b; Wall and McFadden, 2007a). It was unknown whether a shorter duration or altered timing of frequent milking during early lactation would still elicit a persistent effect on milk production; however, because any costs associated with extra labor are increased only during frequent milking, it was of great interest to shorten the duration of frequent milking if a persistent increase in milk yield could still be observed. To answer this question, we assigned cows to UFM (4X of the right udder half, 2X of the left udder half) for d 1 to 14 or d 7 to 21 of lactation (Wall and McFadden, 2007b). We observed an acute milk yield response in both treatments and a significant carryover effect in the d 7 to 21 group. There was a numerical carryover for the d 1 to 14 group; however, it was not significant. Our results indicate that within the first 21 DIM, an interval of frequent milking as short as 2 wk can elicit a persistent increase in milk production. Further narrowing of this window within the first 21 d of lactation, as well as characterization of the cellular response, could provide insight into the mechanisms underlying the receptiveness of the mammary gland to stimulus during this time.

ENDOCRINE RESPONSE TO FREQUENT MILKING

It has long been thought that the hormones released at milking may be involved in regulating the galactopoietic effects of frequent milking on milk production. Indeed, multiple hormones are released during milking including glucocorticoids, oxytocin, and prolactin (**PRL**; Tucker et al., 1975; Carruthers and Hafs, 1980; Akers and Lefcourt, 1982). Along with enhanced milk production, Bar-Peled et al. (1995) observed increased concentrations of GH, IGF-I, oxytocin, and PRL in circulation of cows that were frequently milked or suckled. In addition, the magnitude of milking-induced PRL release declines concomitantly with the decrease in milk production as lactation progresses (Koprowski and Tucker, 1973). Consequently, PRL has been hypothesized as a candidate regulator of the effects of frequent milking on milk production (Dahl et al., 2004a). In an attempt to determine whether milking-induced PRL release indeed mediates the effects of frequent milking on milk production, we assigned cows to 2X, 4X, or 2X plus twice-daily injections of PRL (Crawford et al., 2004; Wall et al., 2006). Four times daily milking or PRL injections increased milk production relative to 2X (Crawford et al., 2004); however, our results indicated that PRL injection or frequent milking exerted distinct effects on mammary cell growth and gene expression and thus probably increased milk production via separate mechanisms (Wall et al., 2006). The response to UFM during early lactation supports this concept; frequent milking may stimulate milk production via local factors, whereas PRL injections may increase milk yield through a more systemic pathway.

CELLULAR RESPONSE TO FREQUENT MILKING

Several authors have speculated that frequent milking increases milk yield via an increase in mammary cell number and (or) activity (Bar-Peled et al., 1995; Stelwagen and Knight, 1997; Sanders et al., 2000; Hale et al., 2003), both of which are critical to improved lactational performance (Capuco et al., 2003). Hillerton et al. (1990) observed an increase in activity of mammary enzymes, protein and lactose synthesis (in heifers only), DNA synthesis, and alveolar area in response to increased milking frequency and concluded that cellular differentiation and proliferation were optimized with frequent milking. Hale et al. (2003) reported an increase in mammary cell proliferation at 7 DIM in cows that were milked 4X for the first 3 wk of lactation compared with cows milked 2X; however, differences in proliferation were only observed in 1 of the 2 frequently milked cow groups. In contrast to those experiments, Norgaard et al. (2005) reported that despite an increase in milk yield (+18%), there was no effect of frequent milking on cell death, proliferation, or enzyme activities in the mammary gland. In agreement with that report, we observed that relative to 2X, 4X did not affect mammary epithelial cell proliferation at 7 DIM (Wall et al., 2006). We did observe an increase in proliferation of stromal cells, however; an increase in mammary expression of suppressor of cytokine signaling (**SOCS**)-2; and a decrease in SOCS-3 expression in response to 4X or PRL injection (Wall et al., 2006). The SOCS are induced in response to PRL, GH, and leptin, as well as cytokines including interleukins and interferon-γ (Aman and Leonard, 1997; Larsen and Ropke, 2002). They act through negative feedback to modulate the signaling of cytokines that use the Janus kinase-signal transducers and activators of transcription pathway (Aman and Leonard, 1997; Larsen and Ropke, 2002). Expression of SOCS-3 in mammary tissue is regulated by milk accumulation in the mammary gland of mice, and it is thought that SOCS-3 may be involved in the inhibition of milk secretion during milk stasis (Tam et al., 2001). The SOCS genes have also been linked to mammary development during the transition period of dairy cows (Wall et al., 2005), mammary cell apoptosis (Le Provost et al., 2005), and proliferation (Robinson et al., 2007). The role of SOCS in the bovine mammary gland is still unclear, and research in this area has revealed the complexity of their action in the mammary gland, as well as the diversity in the regulation and actions of different SOCS family members. The response of these genes to milk removal is very intriguing, and clarification of the physiological and hormonal regulation of SOCS expression will be critical to identifying their role in the mammary gland and its response to milking frequency.

What is unique to early lactation, when the stimulus of frequent milking for a short duration can stimulate a persistent increase in milk production? This question remains unanswered, but work by Stelwagen and Knight (1997) has provided some clues. Using a half-udder model, they compared once-daily milking to 2X of cows in early or late lactation and reported a more dramatic increase in milk secretion efficiency in response to 2X during early lactation compared with late lactation (Stelwagen and Knight, 1997). It is possible that during early lactation, there are more secretory cells present in the mammary gland, and these cells may have more potential to respond to stimulus than cells present in late lactation. Frequent milking may prevent otherwise unused cells from undergoing apoptosis or may provide the stimulus to push the cells to reach greater levels of differentiation, secretory capacity, or both. These scenarios could result in an increase in the number of cells in the gland throughout lactation, an increase in the activity of cells throughout lactation, or both. Shorten et al. (2002) proposed a hypothetical model by which frequent milking for the entire lactation increases the number of active alveoli by reducing the rates of quiescence and senescence in the mammary gland. If such an event occurs with frequent milking during early lactation, this could permanently increase the number of actively secreting alveoli and enhance milk production potential for the remainder of lactation. Many of the biopsy studies that have been previously conducted could have captured changes in mammary cell activity but would not have captured changes in total cell number or in rates of quiescence and senescence within the gland.

CONCLUSIONS

Research in the area of frequent milking of dairy cows has established a robust milk yield response to increased milking frequency and has identified a window of time during early lactation wherein the mammary gland is especially responsive to the stimulus of frequent milking. In addition, there is now evidence that this response is regulated within the mammary gland. The opportunity now exists for dairy scientists to identify the mechanisms involved in local regulation of milk production potential and for dairy producers to further refine milking management practices to maximize milk production efficiency of their operations.

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