Effect of Pathogen-Specific Clinical Mastitis on Milk Yield in Dairy Cows

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ABSTRACT

Our objective was to estimate the effects of the first occurrence of pathogen-specific clinical mastitis (CM) on milk yield in 3071 dairy cows in 2 New York State farms. The pathogens studied were *Streptococcus* spp., *Staphylococcus aureus*, *Staphylococcus* spp., *Escherichia coli*, *Klebsiella* spp., *Arcanobacterium pyogenes*, other pathogens grouped together, and “no pathogen isolated.” Data were collected from October 1999 to July 2001. Milk samples were collected from cows showing signs of CM and were sent to the Quality Milk Production Services laboratory at Cornell University for microbiological culture. The SAS statistical procedure PROC MIXED, with an autoregressive covariance structure, was used to quantify the effect of CM and several other control variables (herd, calving season, parity, month of lactation, J-5 vaccination status, and other diseases) on weekly milk yield. Separate models were fitted for primipara and multipara, because of the different shapes of their lactation curves. To observe effects of mastitis, milk weights were divided into several periods both pre- and postdiagnosis, according to when they were measured in relation to disease occurrence. Another category contained cows without the type of CM being modeled. Because all pathogens were modeled simultaneously, a control cow was one without CM. Among primipara, *Staph. aureus*, *E. coli*, *Klebsiella* spp., and “no pathogen isolated” caused the greatest losses. Milk yield generally began to drop 1 or 2 wk before diagnosis; the greatest loss occurred immediately following diagnosis. Mastitic cows often never recovered their potential yield. Among older cows, *Streptococcus* spp., *Staph. aureus*, *A. pyogenes*, *E. coli*, and *Klebsiella* spp. caused the most significant losses. Many multipara that developed CM were actually higher producers before diagnosis than their nonmastitic herd-mates. As in primipara, milk yield in multipara often

began to decline shortly before diagnosis; the greatest loss occurred immediately following diagnosis. Milk loss persisted until at least 70 d after diagnosis for *Streptococcus* spp., *Klebsiella* spp., and *A. pyogenes*. The tendency for higher producing cows to contract CM may mask its impact on cow health and production. These findings provide dairy producers with more information on which pathogen-specific CM cases should receive treatment and how to manage these cows, thereby reducing CM impact on cow well being and profitability. (**Key words:** pathogen, mastitis, milk yield, mixed model)

Abbreviation key: CI = confidence interval, CM = clinical mastitis.

INTRODUCTION

Mastitis is a common disease in dairy herds in many different countries (e.g., Bigras-Poulin et al., 1990; González et al., 1990; Rajala-Schultz et al., 1999b). It can be challenging to deal with, as it is caused by a wide range of different pathogens. Mastitis can be very detrimental to a dairy farm's profitability, in terms of lost production (e.g., Houben et al., 1993; Rajala-Schultz et al., 1999b; Wilson et al., 2004) and treatment costs (e.g., Hoblet et al., 1991; Miller et al., 1993). A mastitic cow may produce less milk, and what she does produce may not be sold. A dairy producer may simply decide it is more economical to cull a mastitic cow than to treat her, if she does not regain her full production potential.

Mastitis in dairy cows may be caused by a large number of bacterial pathogens. Studies on the pathogenesis and epidemiology of a number of these pathogens have been published and clearly show a difference between pathogens in pathogenesis, epidemiology, and clinical presentation (Montgomery et al., 1987; Barkema et al., 1998; Sears and Wilson, 2003). However, relatively little has been published on pathogen-specific patterns of milk production loss. Among others, Deluyker et al. (1991) and Bartlett et al. (1991) studied milk production loss caused by mastitis using daily milk weights, but too few observations were present to differentiate losses

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by pathogen. Some recent publications have attempted to quantify pathogen specific SCC patterns (de Haas et al., 2002; Djabri et al., 2002). These patterns may aid in the explanation of observed milk production losses per pathogen.

We have recently applied the technique of mixed linear models to study the effect of clinical mastitis (CM) without specific pathogen identification on milk yield in both Finnish (Rajala-Schultz et al., 1999b) and New York State (Wilson et al., 2004) dairy herds. In the Finnish study, milk losses in the first 2 wk after diagnosis ranged from 1.0 to 2.5 kg/d, and the total loss over the entire lactation ranged from 110 to 552 kg, depending on parity and time of mastitis occurrence. In the New York study, milk losses because of CM in parity 1 cows were 5 to 7 kg/d in the first 2 wk after diagnosis and 690 kg over the entire lactation. Among older cows, milk losses because of CM in the first 2 wk following diagnosis ranged from 6 to 9 kg/d and 570 kg over the entire lactation. However, among these older cows, many mastitic cows were higher producers before disease onset than their nonmastitic herd mates, having a potential daily advantage of 2.6 kg. Therefore, the total lactational loss among parity 2+ cows in the Wilson et al. (2004) study is more accurately estimated as 1155 kg. Thus, when studying the effect of a disease on milk yield, it is important to look at repeated measures of milk yield (e.g., daily, weekly, monthly), rather than one single summary measure for the 305-d lactational milk yield (Gröhn et al., 1999) because milk loss will vary with both stage of lactation and time since diagnosis.

Some types of mastitis are more virulent than others, depending on which pathogen has caused the infection. For example, *Mycoplasma* spp., *Arcanobacterium pyogenes*, *Pasteurella* spp., *Klebsiella* spp., and *Enterobacter* spp. have previously been found to cause major milk production losses (Wilson et al., 1997). The severity of milk losses may well differ, depending on which pathogens are involved. Therefore, it is necessary to study pathogen-specific losses, to determine which pathogens have the greatest impact on cow health, production, and profitability. In this study, our objective was to estimate the effects of the first occurrence of CM caused by specific pathogens (*Streptococcus* spp., *Staphylococcus aureus*, *Staphylococcus* spp., *Escherichia coli*, *Klebsiella* spp., *Arcanobacterium pyogenes*, "no pathogen isolated," and "other minor pathogens") on weekly milk production in 2 large New York State dairy herds.

MATERIALS AND METHODS

Herd Descriptions

From October 1, 1999 to July 31, 2001, data for this study were collected from 2 Holstein dairy herds in

New York State. Farm management used a computer program to record lactation, reproductive, and medical data for each cow. Information on parity, milk production, bacterial cultures, SCC, diseases, reproductive status, calving, and culling were readily available. On both farms, each milking unit had milk meters capable of automatically recording milk production, milk conductivity, and the cow activity (measured by a pedometer) and relayed this information to a central databank (S.A.E. Afikim, Kibbutz Afikim, Israel). Both herds were tested monthly by Northeast DHIA for milk production, butterfat, protein, and SCC. All groups of cows in both dairies were fed a balanced, TMR via feed alleys with headlocks that allowed restraint of cows for examination and administration of treatments, medications, and recombinant bST (Monsanto Co., St. Louis, MO). Sick cows were treated according to similar protocols in both herds.

Farm A, located in northern New York, maintained an average of 650 Holstein milking cows, with 1277 calvings between March 1997 and July 2001. Cows were housed in covered barns with concrete floors and free stalls and were classified by lactation, production, and reproductive status into 6 milking groups. These included 3 first lactation cow groups (cows that were 7 to 30 DIM, cows >30 DIM to be bred, and pregnant cows), a mature cow (≥ 2 lactations) group at 7 to 30 DIM, a group of pregnant mature cows >30 DIM and cows (primiparous and multiparous) that had difficulty conceiving, and a hospital group made up of treated cows and recently calved (<7 DIM) cows (primiparous and multiparous). During the course of the study, bedding (paper sludge, shredded dry paper, or kiln-dried sawdust) was added to the stalls every 3 d. The backs of the stalls were raked twice a day during the daylight milkings; only the manure-soiled stalls were raked during the night milking. Manure was scraped from alleys daily. When they were close to calving, nonlactating cows were moved to a loose housing maternity pen bedded with straw. Animals were housed for the first week of their lactation in a large pen with a sand and sawdust combination for bedding; this pen was cleaned out weekly. After 1 wk of lactation, cows were moved to an adjacent 60-stall free stall facility and kept in smaller groups until they were 30 DIM.

Cows were milked in a double-12 parallel parlor 3 times/d. Milk meters recorded individual cow milk production, which was stored in a computerized database (S.A.E. Afikim). The rolling herd average was 11,588 kg per cow/yr on a 305-d basis; monthly mean SCC was 225,000 cells/mL (range, 180,000 to 355,000).

Some cases of CM were identified by the milkers when drying udders. Others were detected by the herds persons examining cows whose milk electrical conductivity

increased by >15% when compared with their previous 7-d rolling average and had a concurrent decrease in milk production. Decreases in milk production that triggered a mastitis diagnosis were 15% from one milking to the next for cows <41 DIM, 20% for cows between 41 and 120 DIM, and 40% for cows >120 DIM. Cows in the first 30 d of lactation were observed particularly closely in their smaller group for any type of infection and ketosis.

Farm B, located in western New York, had 830 milking cows at the beginning of the study and expanded to 1120 milking cows by the end of the study. On Farm B, there were 1794 calvings between October 1996 and March 2001. Milking cows were housed in recently built covered free stall barns with concrete floors and divided into 7 milking groups by lactation, production, and reproductive status. These included a first lactation cow group and 4 groups with mature cows (≥ 2 lactations), a recently calved cow group (up to 30 DIM), and a treated group. Stalls were raked 3 times/d. Fresh sawdust bedding was added to free stalls 2 times/wk. Dry cows were housed in an old free stall barn, in which ventilation, stall condition, and sawdust bedding were adequate. Two weeks before she was due to calve, each cow or prefresh heifer was moved to a loose housing calving area bedded with chopped newspaper. Cows were returned to free stall housing 2 d after calving. First lactation cows were moved to their own group for the remainder of their first lactation. Mature cows entered the fresh cow group until they were 30 DIM, after which they went into one of the 4 mature cow groups. Cows were milked 3 times/d in a double-24 herringbone parlor. This farm used the same individual cow milk production and electrical conductivity recording system as Farm A.

The CM cases were identified by milkers when drying udders or by detecting changes in electrical conductivity, cows' walking (pedometer activity), or milk production compared with the average of the previous 7 d. When 2 of the following conditions were satisfied, the cow went on mastitis alert status: electrical conductivity increase >30%, pedometer activity decrease >40%, milk production increase <7% for cows 1 to 45 DIM, production decrease >20% for cows 46 to 114 DIM, production decrease >17% for cows 115 to 199 DIM, production decrease >35% for cows >199 DIM. Any cow with milk production <9 kg/d was placed on mastitis alert status. The CM cases were divided into 2 groups, according to farm definitions: those that the employees judged were "coliform mastitis" and those that were not. "Non-coliform cows" were defined as those with only local involvement of the mammary gland, such as moderate swelling; normal or discolored, but not watery, milk; rectal temperatures $\leq 39.7^\circ\text{C}$, and normal

eating behavior. Cases judged as "coliform mastitis" had marked swelling of mammary quarters and/or thin or watery milk and were accompanied by systemic signs of disease such as appetite loss and rectal temperature $>39.7^\circ\text{C}$. During the study, mean milk production per cow was 10,182 kg/yr, and monthly mean bulk milk SCC was 240,000 cells/mL (range, 170,000 to 310,000).

Data Collection

At the initial herd visits, a questionnaire was completed on each farm to collect data on mastitis control and other management policies related to udder health in the herd. This included information on milking herd housing, milking procedures, dry cow and lactating cow therapy, culling of cows with repeated cases of CM, milking machine maintenance and performance test results, and milk production and quality information. Herd managers and milkers were instructed on aseptic collection and handling of milk samples. Written instructions and color code-labeled containers were left at each farm for sample collection. A schedule was arranged for milk samples and records to be picked up twice a week. Milk samples for microbiological diagnosis were frozen at -25°C after collection.

Working with all farm personnel who were expected to collect data, case definitions were standardized for all 9 diseases being studied. Aseptically collected milk samples were cultured from each milking cow at the beginning of the study to characterize the study herds. Monthly SCC at the cow and herd levels were also recorded. Milk samples were aseptically collected and cultured from cows at clinical onset during every episode of CM that occurred during the study period. Data were collected from October 1, 1999 to July 31, 2001 for Dairy A and from October 1, 1999 to March 31, 2001 for Dairy B. Data collection was started earlier on Dairy B, but some early data were discarded because of technical problems with accurate identification of cows by the milk weight recording system. These problems were corrected by October 1, 1999.

Case Definition

All lactating cows in the 2 study herds were eligible for inclusion as cases of CM. All milkers on the cooperating farms were familiar with detection of CM by examination of foremilk. Nevertheless, training and standardization concerning CM detection was provided at the beginning of the study. Farm personnel collected samples for microbiological culture from quarters with signs of CM.

Some cows had 2 clinical episodes in the same quarter within several days of each other. Any such episode

that occurred within 5 d of end of treatment (or end of milk withholding) was considered a chronic case of mastitis. Any episode that occurred from 6 to 14 d after recovery from the earlier episode was considered chronic if the same etiologic agent was isolated from both episodes. If a different mastitis pathogen was isolated, it constituted a new CM case. Any episode that occurred more than 14 d after recovery was considered a new CM case.

Microbiological Procedures

Recommended procedures for diagnosis of bovine IMI were followed (Hogan et al., 1999). Milk samples were plated by streaking 0.01 mL on trypticase soy agar II with 5% sheep blood and 0.1% esculin (BBL; Becton Dickinson Microbiology Systems, Cockeysville, MD). Plates were incubated at 37°C for 48 h. After observation of colony morphology and hemolytic patterns on blood agar, isolates were examined further by means of 3% KOH, gram-staining of organisms, catalase and oxidase testing, and additional biochemical and metabolic evaluations as needed. Colony morphology on MacConkey agar and the BBL Crystal ID System (Becton Dickinson) identified gram-negative organisms. Streptococci that had a negative CAMP reaction were classified as *Streptococcus* spp. Staphylococci with β or $\alpha\beta$ hemolytic patterns that had a positive tube test for free coagulase were classified as *Staph. aureus*. Nonhemolytic staphylococci with a positive tube coagulase test were further identified with the API Staph System (bioMérieux Vitek, Hazelwood, MO). Coagulase-negative staphylococci were classified as *Staphylococcus* spp.

Between 8 and 38% of samples from cows with CM might have had a negative culture when the previously described standard method was used (Anderson et al., 1982; González et al., 1990; Sears et al., 1993). Therefore, after the primary culture was performed, 2-mL aliquots of all CM samples were inoculated for 4 h at 37°C in a water bath with equal amounts of Todd-Hewitt broth (Unipath Co., Oxoid Division, Ogdensburg, NY) and recultured on blood agar and MacConkey plates. We had already used this method and obtained the greatest improvement in sensitivity for recovery of mastitis pathogens without a concomitant increase in contamination (Dinsmore et al., 1992; Sears et al., 1993). In samples from CM cases, isolation of only one type of microorganism from a preincubated quarter sample suggested a true infection. If more than one type of organism were isolated, it was considered a contaminated sample, except when isolates present on the plate included *Staph. aureus*. From our experience, isolates of *Staph. aureus* from preincubated samples originate in the mammary gland if the organism was

not isolated on primary culture. All bacterial isolates from CM cases were kept frozen in the laboratory at -80°C.

Other Diseases

Although focusing on CM, we also chose 8 other diseases for inclusion in the models as potential confounders. These 8 diseases are among the most common clinical conditions that are universally a problem in dairy cows, have a reasonable basis for influencing replacement decisions, and occur at least in part because of management decisions. The rationale for choosing them is that they may also cause milk loss in addition to the effects of CM.

The 8 recorded diseases (in addition to CM) were dystocia, milk fever, retained placenta, metritis, ketosis, displaced abomasum, lameness, and cystic ovarian disease. They were defined as follows. Dystocia was a calving that required farmer or veterinary assistance. Milk fever occurred if a cow was unable to rise or had cool extremities and sluggish rumen motility near the time of calving, but was treated successfully with calcium. Retained placenta was retention of fetal membranes for at least 24 h postcalving. Metritis involved a febrile state accompanying a purulent or fetid vaginal discharge or a diagnosis of an enlarged uterus by veterinary palpation. Ketosis was diagnosed by a drop in feed intake and milk production; detection of ketones in milk, urine, or breath; no other concomitant diseases; and response to treatment. Displaced abomasum occurred when the abomasum was enlarged with fluid, gas, or both and was mechanically trapped in either the left or right side of the abdominal cavity. Nearly every displaced abomasum case was confirmed by surgery, but cows removed from the herd without treatment were also recorded. Lameness was limping or abnormal weight bearing. An ovarian cyst was defined as a persistent ovarian structure >25 mm in diameter and associated with anestrus or erratic estrus behavior. Every effort was taken to ensure that disease definition and diagnostic criteria were the same in both herds. Written disease definitions were provided to dairy producers and veterinarians involved.

Statistical Methods

The SAS procedure PROC MIXED (SAS, 1999) was used to study the effects of the mastitis pathogens and several control variables (herd, calving season, parity, month of lactation, vaccination status, other diseases) on weekly milk yield in 3071 cows in 2 farms. These variables were all considered fixed, i.e., the estimates of their effects on milk yield applied only to the data

analyzed here, but were not extrapolated to a larger population.

The outcome variable, weekly milk yield, was calculated as follows: the milk weights were collected and recorded 3 times daily, i.e., at each milking. They were then summed to give a daily value. Then, within each week of lactation, the 7 daily values were summed and divided by 7 to give the mean daily milk yield for that particular week in lactation. This was done to reduce the impact of any randomly occurring zero-values for a particular milking, e.g., if a cow missed one milking for some reason other than being in the sick pen.

Because our data set contained repeated measurements of milk yield within a cow over her lactation and these were correlated with one another, it was important to incorporate this feature into the model. This is accomplished in SAS PROC MIXED (SAS, 1999) by specifying a correlation structure among the repeated measurements; several different structures are available. In previous work, we compared the simple, compound symmetry, and autoregressive (Order 1) structures (Rajala-Schultz et al., 1999a) and simple, compound symmetry, autoregressive (Order 1), Toeplitz (Order 5), and unstructured structures (Wilson et al., 2004) to measure the effects of diseases on milk yield. In both studies, the autoregressive (Order 1) structure, in which correlations between adjacent repeated milk measurements were higher than between measurements further apart, resulted in the best model fit, based on various goodness-of-fit measures, including Akaike's information criterion and the Bayesian information criterion. Indeed, it is biologically reasonable to assume that milk weights measured in the same stage of lactation are more highly correlated than those measured further apart in time. Therefore, in the study reported here, an autoregressive (Order 1) covariance structure was fitted. One may argue that an unstructured covariance structure might be more appropriate, because each pair of measurements has its own correlation. However, our main concern lay in the point estimates, which do not change much between structures. Therefore, choice of covariance structure is not of great consequence; the variance components may differ, but these were not our main interest. The subject effect was an individual cow; including this term in the model ensured that all of a particular cow's milk weights, which were not independent because they occurred within the same cow, were assigned to her, and not to some other cow.

Calving season had 4 categories: December through February, March through May, June through August, and September through November. Parity was divided into 2 groups, which were analyzed separately: first and second and higher; within the older group, parity

was further subdivided into parities 2, 3, and 4+. Milk yields were modeled for the first 50 wk of lactation.

The mastitis pathogens studied were *Streptococcus* spp., *Staph. aureus*, *Staphylococcus* spp., *E. coli*, *Klebsiella* spp., and *A. pyogenes*. In addition, a variable for clinical cultures from which no pathogen was isolated was created. Lastly, a variable that included all other, less common pathogens isolated from the cows in the study was created. These "other pathogens" included *Pasteurella* spp., *Proteus* spp., *Serratia* spp., gram-negative *Bacillus*, *Yeast*, gram-positive *Bacillus*, *Corynebacterium* spp., *Enterobacter* spp., *Citrobacter* spp., and *Strep. canis*.

The first episode during lactation of CM caused by each etiologic agent of interest was studied; therefore, cows could contribute more than one case to the study. The most recent lactation during the study period was used because that was the lactation for which complete daily milk weights could be retrieved. The other diseases controlled for in the models were dystocia, retained placenta, milk fever, metritis, displaced abomasum, ketosis, lameness, and cystic ovary.

For each disease, an index variable was created to classify the milk weights according to when they were measured in relation to disease occurrence (see Table 1 for the index values for a sample mastitic cow). This enabled us to precisely determine when a disease had an effect on milk yield. For each mastitis pathogen, the index variable had 17 levels: one pertained to cows that did not have mastitis caused by that specific pathogen. The remaining index levels (for mastitic cows only) pertained to milk yields recorded ≥ 29 d, 22 to 28 d, 15 to 21 d, 8 to 14 d, and 1 to 7 d before mastitis and 0 to 7 d, 8 to 14 d, 15 to 21 d, 22 to 28 d, 29 to 35 d, 36 to 42 d, 43 to 49 d, 50 to 56 d, 57 to 63 d, 64 to 70 d, and ≥ 71 d after diagnosis of mastitis. The other diseases controlled for in the models had between 6 and 12 levels, relating milk yield to time of disease occurrence. For each index, the level representing cows without the disease was the reference category, so all milk losses resulting from a disease were compared with milk yields of cows without the relevant disease.

For cows at second parity or greater, the following model was used:

$$Y = \text{herd} + \text{parity} + \text{calving season} + \text{week in milk} + \text{vaccination status} + \text{dystocia} + \text{retained placenta} + \text{milk fever} + \text{metritis} + \text{displaced abomasum} + \text{ketosis} + \text{lameness} + \text{cystic ovary} + \text{Streptococcus spp.} + \text{Staph. aureus} + \text{Staphylococcus spp.} + \text{E. coli} + \text{Klebsiella spp.} + \text{A. pyogenes} + \text{"no pathogen isolated"} + \text{"all other pathogens"} + e$$

where Y is the mean milk yield per day in a particular week of lactation (as defined earlier), the independent

Table 1. Values of mastitis index variable for sample mastitic cow for analyzing effect of mastitis on milk yield.

Day in milk	Day of mastitis	Mastitis index ¹
Any	Not applicable	0
4	42	1
11	42	1
18	42	2
25	42	3
32	42	4
39	42	5
46	42	6
53	42	7
60	42	8
67	42	9
74	42	10
81	42	11
88	42	12
95	42	13
102	42	14
109	42	15
116	42	16
123	42	16

¹Values of mastitis index are interpreted as follows: 0 = milk yields recorded on cows that did not contract the type of clinical mastitis under study, 1 = milk yields recorded ≥ 29 d before diagnosis of mastitis, 2 = milk yields recorded 22 to 28 d before diagnosis, 3 = milk yields recorded 15 to 21 d before diagnosis, 4 = milk yields recorded 8 to 14 d before diagnosis, 5 = milk yields recorded 1 to 7 d before diagnosis, 6 = milk yields recorded 0 to 7 d after diagnosis, 7 = milk yields recorded 8 to 14 d after diagnosis, 8 = milk yields recorded 15 to 21 d after diagnosis, 9 = milk yields recorded 22 to 28 d after diagnosis, 10 = milk yields recorded 29 to 35 d after diagnosis, 11 = milk yields recorded 36 to 42 d after diagnosis, 12 = milk yields recorded 43 to 49 d after diagnosis, 13 = milk yields recorded 50 to 56 d after diagnosis, 14 = milk yields recorded 57 to 63 d after diagnosis, 15 = milk yields recorded 64 to 70 d after diagnosis, and 16 = milk yields recorded ≥ 71 d after diagnosis.

variables are as defined previously, and e is an error term representing within-cow correlation of milk weights. Because all pathogens were included simultaneously in the same model, a control cow was one without a diagnosis of CM. For first parity cows, the same model was used, except that the terms for parity and vaccination status were omitted, as they were not applicable.

The repeated observations in the study are the milk weights. Each milk weight is uniquely identified by the combination of the 2 fixed, independent effects of week in milk and each bacteria-specific mastitis index. These 2 effects indicate the temporal relationship between an individual milk weight and mastitis occurrence (mastitis index) and the time of its measurement (week in milk). Thus, although a cow may appear more than once in an extreme index (≥ 29 d before diagnosis or ≥ 71 d after diagnosis) or in the category representing no mastitis, the inclusion of week in milk (along with mastitis index) in the model ensures that each milk weight is uniquely identified. Each week in milk contained only one milk weight per cow, representing, as described

previously, the mean daily milk yield in that week. A similar explanation applies to the other disease indices.

Parity 1 ($n = 1038$) and parity 2+ ($n = 2033$) cows were analyzed separately, because of the greatly differing shapes of their lactation curves. After restricting the lactation follow-up period to the first 50 wk in milk in the mixed model analysis, there were 1028 parity 1 cows and 2004 parity 2+ cows. In the analysis on parity 1 cows, there were 24,411 weekly milk weights used. In the analysis on parity 2+ cows, there were 44,929 weekly observations used.

Further technical details, with a practical example, of mixed models are available in (Gröhn et al., 1999).

RESULTS AND DISCUSSION

Descriptive Findings

Table 2 gives the lactational incidence risk, number, and median and mean DIM (and range) of clinical cases for each farm in the study by parity group (1, and 2+) and for each pathogen studied. *Escherichia coli* was the most commonly isolated pathogen, followed by *Streptococcus* spp. "No pathogen isolated" was also a fairly common finding. For all pathogens studied, the incidence of CM was higher in Herd A than in Herd B. This result might be due in part to different farm management. Herd B did not routinely forestrip for abnormal milk, so they collected relatively fewer cases of mastitis compared with Herd A. Thus, less severe cases, which may not be of such great economic or veterinary importance, were less likely to be recorded. For all pathogens, the incidence of CM was higher among older cows than those in parity 1 in both herds.

Cases of CM occurred throughout lactation. Although the median day of lactation for diagnosis of most cases occurred in midlactation, many cases were diagnosed in the first part of lactation, particularly among parity 1 cows. These findings are in line with previously reported observational studies (i.e., Erskine et al., 1988; Hogan et al., 1989; Bigras-Poulin et al., 1990; González et al., 1990; Barkema et al., 1998). For most pathogens in the current study, CM tended to occur earlier in lactation in parity 1 cows than in parity 2+ cows. For some pathogens, the median DIM as shown in Table 2 may differ from that shown in the figures, because we restricted analysis of milk yield to the first 50 wk in lactation; thus, we had slightly fewer cows available for analysis (3032 vs. 3071).

Table 3 presents the lactational incidence risks of the other diseases controlled for in the models estimating milk loss within each farm. On both farms, dystocia and metritis were more common in parity 1 cows than in older cows. The lactational incidence risk for most diseases was higher in Farm A than in Farm B.

Table 2. Lactational incidence risk (number of clinical cases) and median and mean days in milk (and range) of first occurrence of bacteria-specific mastitis by parity group in each of 2 New York State dairy herds.

		Pathogen							
	Parity	<i>Streptococcus</i> spp.	<i>Staphylo-</i> <i>coccus</i> <i>aureus</i>	<i>Staphylo-</i> <i>coccus</i> spp.	<i>Escherichia</i> <i>coli</i>	<i>Klebsiella</i> spp.	<i>Arcanobacterium</i> <i>pyogenes</i>	None isolated	All others
Lactational incidence risk (number of clinical cases)									
Farm A (n = 1277)	1	6.2% (23)	1.9% (7)	2.4% (9)	5.6% (21)	0.8% (3)	0.5% (2)	4.0% (15)	0.5% (2)
	2+	8.3% (75)	4.3% (39)	2.3% (21)	8.4% (76)	4.8% (43)	2.4% (22)	8.5% (77)	2.0% (18)
Farm B (n = 1794)	1	0.9% (6)	0.9% (6)	0.6% (4)	1.5% (10)	0.8% (5)	0.0% (0)	1.5% (10)	0.8% (5)
	2+	2.8% (31)	1.5% (17)	2.1% (23)	3.7% (41)	3.1% (34)	1.0% (11)	2.4% (26)	0.9% (10)
Parity 1 overall (n = 1038)		2.8% (29)	1.3% (13)	1.3% (13)	3.0% (31)	0.8% (8)	0.2% (2)	2.4% (25)	0.7% (7)
Parity 2+ overall (n = 2033)		5.2% (106)	2.8% (56)	2.2% (44)	5.8% (117)	3.8% (77)	1.6% (33)	5.1% (103)	1.4% (28)
Median; mean days in milk (range)									
Farm A	1	1; 55 (1-171)	1; 46 (1-258)	1; 2 (1-4)	76; 100 (1-264)	260; 199 (1-336)	33; 33 (1-64)	12; 32 (1-193)	160; 160 (80-239)
	2+	86; 110 (1-343)	87; 100 (1-282)	74; 94 (1-286)	100; 103 (1-268)	110; 117 (1-325)	1; 70 (1-332)	94; 116 (1-322)	50; 75 (1-223)
Farm B	1	66; 146 (3-269)	88; 98 (37-194)	55; 63 (1-142)	86; 103 (1-263)	108; 105 (38-175)	NA ¹	58; 69 (16-212)	79; 93 (27-206)
	2+	74; 101 (2-269)	98; 96 (1-263)	152; 138 (1-334)	96; 115 (4-334)	100; 121 (17-264)	157; 120 (2-228)	82; 88 (1-235)	119; 129 (28-252)
Parity 1 overall		2; 75	52; 70	2; 21	76; 101	109; 141	33; 33	22; 47	80; 112
Parity 2+ overall		80; 107	93; 99	113; 117	99; 107	101; 119	7; 86	87; 109	81; 94

¹Not applicable; there were no cases of *A. pyogenes* clinical mastitis in parity 1 cows in Farm B.

Table 3. Lactational incidence risk (%) of diseases, other than mastitis, controlled for in the mixed models for milk loss by parity group in each of 2 New York State dairy herds.

	Parity	Disease							
		Dystocia	Retained placenta	Milk fever	Metritis	Displaced abomasums	Ketosis	Lameness	Ovarian cyst
Farm A (n = 1277)	1	38.3	4.3	0.0	14.5	1.3	24.9	15.5	3.5
	2+	15.7	15.5	9.5	6.7	1.9	20.9	20.5	5.2
	Overall	22.3	12.2	6.7	9.0	1.7	22.1	19.0	4.7
Farm B (n = 1794)	1	26.2	8.9	0.0	13.5	2.7	5.3	43.2	0.5
	2	9.0	9.7	1.8	2.5	3.7	5.9	39.3	1.3
	Overall	15.4	9.4	1.1	6.6	3.3	5.7	40.7	1.0

Losses Among Parity 1 Cows

Daily milk losses associated with the first occurrence of each CM pathogen in parity 1 cows are presented in Table 4. This table presents results from a model including all pathogens simultaneously. Figure 1 (A–H) shows the corresponding lactation curves for a non-mastitic and a mastitic cow for each pathogen. For the mastitic cow, diagnosis of CM was assumed to occur on the median DIM of diagnosis of all cows with that pathogen-specific type of CM (indicated by an arrow). For several weeks prior to diagnosis, most mastitic cows had the same milk yield as their nonmastitic herd-mates, which is confirmed by the 95% confidence interval (CI) (Table 4) overlapping zero, which can also be seen in Figure 1 (A–H). In this figure, the lactation curves of the nonmastitic and mastitic cows are virtually identical. However, for some pathogens (*Staph. aureus*, *Staphylococcus* spp., and “no pathogen isolated”), in the week or 2 before diagnosis, milk yield began to drop. Deluyker et al. (1991) reported a similar finding. Their study did not differentiate by pathogen, but observed an identical prediagnosis milk drop. In our study, there was milk loss for several weeks after diagnosis for all pathogens reported here. The loss was substantial in cows with *Staph. aureus*, *E. coli*, *Klebsiella* spp., and “no pathogen isolated” CM. Our findings are reported in detail subsequently.

***Streptococcus* spp.** Parity 1 cows infected with *Streptococcus* spp. experienced only a slight drop in milk production after disease onset (Figure 1A). The largest, and only significant, drop, 2.5 kg/d, occurred in the first week after diagnosis (Table 4). The median time of diagnosis was 2 DIM, so most losses occurred early in lactation. These mastitic cows appeared to fully recover, in terms of their milk production, as can be seen in the latter part of the lactation curve, when they surpassed, albeit only slightly, the production of their noninfected herd-mates. It would appear that milk production in parity 1 cows was not adversely affected by *Streptococcus* spp. beyond 1 wk after diagnosis.

***Staphylococcus aureus*.** The median DIM of diagnosis for *Staph. aureus* among parity 1 cows on these 2 farms was 52. Until 1 to 2 wk before diagnosis, milk production was not affected by this pathogen. However, after that point, milk production in these cows dropped sharply and never quite recovered, at least in the 70 d following diagnosis (Figure 1B). Cows with *Staph. aureus* produced about 8.4 kg less milk/d in the first 2 wk following diagnosis (Table 4). Over the next several weeks, production slowly improved but was still significantly below that of cows not infected with *Staph. aureus*. This pathogen appeared to be quite detrimental to milk yield, as parity 1 cows infected with it experienced significant milk losses in most of the 10 wk following diagnosis.

***Staphylococcus* spp.** Parity 1 cows were diagnosed with *Staphylococcus* spp. at a median DIM of 2. Their lactation curve was parallel to, but slightly lower than, that of cows not infected with *Staphylococcus* spp. (Figure 1C). The largest drop (3.2 kg/d) occurred in the week immediately following diagnosis; however, this loss was not statistically significant (Table 4). After that, daily losses fluctuated between 1 and 3 kg/d. Although the losses were not statistically significant, the upper boundary of the 95% CI in most weeks was only slightly greater than zero, with most of the interval lying below zero.

***Escherichia coli*.** *Escherichia coli* infection was diagnosed at a median of 76 DIM in parity 1 cows (Figure 1D). Cows with *E. coli* produced 6.7 kg less milk/d in the first week after diagnosis and approximately 5 kg less milk/d in the following 3 wk (Table 4). Then, over the next several weeks, cows lost between 1.5 and 3.4 kg/d of milk, compared with cows that did not have *E. coli* mastitis. Therefore, *E. coli* appeared to be an economically significant pathogen in young dairy cows, as milk loss was quite substantial over the lactation and never recovered. The relatively strong impact of *E. coli* on milk production may be expected given the pathogenesis of this infection and the observed severity in SCC increase during infection (De Haas et al., 2002).

Table 4. Effects of first occurrence of bacteria-specific clinical mastitis on milk yield of 1028 parity-1 cows in 2 New York State dairy farms. Estimates were obtained from a mixed model with an autoregressive (Order 1) covariance structure.¹ Values are kilograms of milk/d. CI = confidence interval.

Effect	<i>Streptococcus</i> spp.		<i>Staphylococcus aureus</i>		<i>Staphylococcus</i> spp.		<i>Escherichia coli</i>		<i>Klebsiella</i> spp.		No pathogen isolated		<i>Arcanobacterium pyogenes</i> ³		All other pathogens	
	Est. ²	95% CI	Est.	95% CI	Est.	95% CI	Est.	95% CI	Est.	95% CI	Est.	95% CI	Est.	95% CI	Est.	95% CI
≤29 d BD ⁴	0.81	-1.3, 2.9	0.97	-2.0, 4.0	-1.95	-7.9, 4.0	0.97	-0.8, 2.7	2.26	-0.8, 5.4	-2.10	-5.0, 0.8	-0.81	...	-3.18	-6.9, 0.6
22–28 d BD	0.22	-2.5, 2.9	-0.94	-4.3, 2.5	-2.78	-9.4, 3.9	1.53	-0.6, 3.7	1.27	-2.4, 5.0	-0.65	-3.6, 2.3	-1.98	...	-2.92	-7.0, 1.2
15–21 d BD	2.62	-0.3, 5.5	-1.11	-4.7, 2.5	-1.48	-8.2, 5.2	2.00	-0.3, 4.3	2.18	-1.8, 6.2	-0.80	-3.6, 2.0	1.82	...	-2.33	-6.7, 2.0
8–14 d BD	0.18	-2.6, 3.0	0.69	-2.9, 4.3	-1.25	-7.4, 4.9	2.55*	0.2, 4.9	0.23	-4.1, 4.5	-0.88	-3.5, 1.8	0.55	...	-2.71	-7.3, 1.9
1–7 d BD	1.04	-1.9, 4.0	-2.71	-6.5, 1.0	0.31	-4.6, 5.2	0.66	-1.7, 3.0	0.21	-4.2, 4.6	-3.26*	-5.8, -0.7	-7.12	...	-3.90	-8.5, 0.7
0–7 d AD ⁵	-2.53*	-4.8, -0.3 ^a	-8.38*	-11.7, -5.1 ^b	-3.23	-6.6, 0.2 ^{ab}	-6.67*	-8.8, -4.5 ^{ab}	-7.63*	-11.9, -3.4 ^{ab}	-7.15*	-9.6, -4.7 ^{ab}	-14.14	...	-7.18*	-11.8, -2.5 ^{ab}
8–14 d AD	-1.15	-3.5, 1.1 ^a	-7.98*	-11.3, -4.7 ^b	-1.60	-5.0, 1.8 ^{ab}	-4.71*	-6.9, -2.5 ^{ab}	-4.72*	-9.2, -0.3 ^{ab}	-7.01*	-9.5, -4.6 ^b	-13.72	...	-5.10*	-9.9, -0.3 ^{ab}
15–21 d AD	-1.69	-4.0, 0.7	-6.37*	-9.8, -2.9	-2.09	-5.5, 1.3	-4.85*	-7.1, -2.6	-4.25	-9.0, 0.5	-6.38*	-8.9, -3.9	-12.53	...	-3.86	-9.0, 1.3
22–28 d AD	-1.67	-4.1, 0.8	-4.37*	-7.9, -0.9	-1.34	-4.8, 2.2	-5.04*	-7.4, -2.7	-2.80	-7.8, 2.2	-5.43*	-8.0, -2.9	...	...	-1.53	-6.8, 3.8
29–35 d AD	-1.07	-3.6, 1.4	-3.53	-7.1, 0.0	-2.28	-5.8, 1.2	-2.72*	-5.1, -0.3	-4.41	-9.7, 0.9	-5.68*	-8.2, -3.1	...	...	-2.54	-7.9, 2.8
36–42 d AD	-1.04	-3.6, 1.5	-5.39*	-8.9, -1.9	-3.22	-6.7, 0.2	-2.71*	-5.2, -0.2	-3.30	-8.7, 2.1	-5.33*	-7.9, -2.8	...	...	-5.81*	-11.2, -0.4
43–49 d AD	-0.44	-2.9, 2.1	-4.48*	-8.0, -0.9	-2.72	-6.2, 0.8	-3.40*	-5.9, -0.9	-6.98*	-12.5, -1.5	-4.07*	-6.6, -1.5	...	...	-2.28	-7.9, 3.3
50–56 d AD	1.08	-1.4, 3.6	-3.66*	-7.1, -0.2	-2.61	-6.1, 0.9	-2.60*	-5.1, -0.1	-6.72*	-12.3, -1.1	-3.48*	-6.0, -0.9	...	...	-0.25	-6.2, 5.7
57–63 d AD	1.17	-1.2, 3.5 ^a	-3.33	-6.7, 0.0 ^{ab}	-3.08	-6.5, 0.3 ^{ab}	-2.20	-4.6, 0.2 ^{ab}	-5.27	-10.9, 0.3 ^{ab}	-4.14*	-6.6, -1.7 ^b	...	...	0.26	-5.7, 6.3 ^{ab}
64–70 d AD	1.09	-1.0, 3.2	-1.83	-5.0, 1.3	-2.10	-5.2, 1.0	-1.45	-3.6, 0.7	-5.17	-11.2, 0.8	-3.22*	-5.6, -0.9	...	...	2.12	-3.7, 7.9
≥71 d AD	0.66	-1.0, 2.3 ^a	-1.79	-4.4, 0.9 ^{ab}	-2.78*	-5.3, -0.3 ^{ab}	-2.00*	-3.9, -0.1 ^{ab}	-5.23*	-10.4, -0.0 ^{ab}	-3.16*	-5.2, -1.2 ^b	...	...	0.59	-4.7, 5.9 ^{ab}

^{a,b}Denote significant differences in milk loss between pathogens in a week relative to diagnosis, as measured by determining whether their 95% CI cross.

¹Other factors controlled for in the model were herd, calving season, week of lactation, and other diseases (dystocia, retained placenta, metritis, displaced abomasum, ketosis, lameness, and cystic ovary).

²Values represent the amount of milk (kg) lost (or gained) per day within the week shown, e.g., cows with *Streptococcus* spp. produced 2.5 kg less milk/d in the week immediately following diagnosis compared with cows without *Streptococcus* spp. A positive value indicates that mastitic cows produced more milk in the week than did nonmastitic cows.

³Too few observations to obtain confidence intervals, or later estimates, for *A. pyogenes*.

⁴BD = Before diagnosis.

⁵AD = After diagnosis.

* $P < 0.05$.

Figure 1. Lactation curves of 2 parity-1 cows. One cow was infected with A) *Streptococcus* spp., B) *Staphylococcus aureus*, C) *Staphylococcus* spp., D) *Escherichia coli*, E) *Klebsiella* spp., F) no pathogen isolated, G) *Arcanobacterium pyogenes*, or H) all other pathogens (Panel H) (—▲—); the other cow was without the corresponding pathogen (---□---). The difference at each point of the lactation curves in each panel corresponds to the estimates in Table 4. The arrow indicates median DIM of diagnosis of the mastitic cow.

***Klebsiella* spp.** Among parity-1 cows, the median day of diagnosis of *Klebsiella* spp. was quite late (109 d). Cows experienced a sharp drop in production in the

first week after diagnosis, recovered somewhat, then experienced another sharp drop 6 wk after diagnosis (Figure 1E). Specifically, daily milk losses in the first

week after diagnosis were 7.6 kg/d, after which they decreased to 3.3 kg/d at 36 to 42 d after diagnosis (Table 4). Then, between 43 and 49 d after diagnosis, cows infected with *Klebsiella* spp. produced 7 kg/d less milk than cows not infected with *Klebsiella* spp. This decrease in production was sustained over the next several weeks; cows with *Klebsiella* spp. continued to produce at least 5 kg less milk/d than cows without *Klebsiella* spp. This pattern of milk loss could be an indication of a secondary infection some time after the first diagnosis was made; unfortunately, we were unable to directly study the effects of more than one occurrence of the same pathogen in a cow. Nevertheless, our results indicate that *Klebsiella* spp. appears to be an important pathogen to focus on in any mastitis control programs in dairy cows, although it can be a very difficult organism to control.

“No pathogen isolated.” Although a specific pathogen could not be isolated from all mastitis cultures, this is an important category to be aware of. Among parity 1 cows in this study that had “no pathogen isolated” from their mastitis cultures, milk loss was quite significant, and persistent after diagnosis at a median of 22 DIM (Figure 1F). There was no significant effect on milk yield until the week before diagnosis when cows lost 3.3 kg of milk/d (Table 4). Cows then lost over 7 kg/d in the first 2 wk after diagnosis. Milk losses remained substantial in the following weeks, ranging from 3.2 to 6.4 kg/d. Morin and Constable (1998) studied these cases in more detail and concluded that a large proportion had very similar characteristics as Gram-negative bacterial infections; González et al. (1990) concluded that negative cultures were mostly from udders infected with coliform bacteria.

***Arcanobacterium pyogenes*.** Cows infected with *A. pyogenes* experienced the greatest milk loss (Table 4; Figure 1G), but these values may be overestimated because of the small sample size (only 2 parity 1 cows had *A. pyogenes*). The median day of diagnosis was 33 DIM. In the second and third weeks prior to diagnosis, cows with *A. pyogenes* produced more milk than cows not infected with *A. pyogenes*. However, 1 wk before diagnosis, the former cows produced 7.1 kg less milk/d than did the latter cows. After diagnosis, the drop in production was more dramatic, but again, was based on milk yields from only 2 cows.

Other minor pathogens. Parity 1 cows infected with a pathogen other than those discussed previously produced less milk throughout lactation than noninfected cows, even 1 mo prior to diagnosis (Table 4; Figure 1H). However, the difference was not significant until the first week after diagnosis, which occurred at a median of 80 DIM. At this time, cows lost 7.2 kg of milk/d. Losses declined until the sixth week following

diagnosis, when they increased to 5.8 kg/d (Table 4), then tapered off again in the following weeks. By 57 d post diagnosis, cows with mastitis caused by one of these pathogens were actually producing more milk than noninfected cows, although the difference was not significant. Significant milk losses caused by these other pathogens occurred only in the first 2 wk after diagnosis and in the sixth week following diagnosis. For parity 1 cows, the pathogens included in this category were *Pasteurella* spp., yeast, *Enterobacter* spp., and *Strep. canis*.

Losses Among Parity 2+ Cows

Daily milk losses associated with the first occurrence of each pathogen in cows of parity 2 and higher are presented in Table 5. The table presents results from a model including all pathogens simultaneously. Figure 2 (A–H) shows the corresponding lactation curves for a nonmastitic and a mastitic cow for each pathogen. In the figure, as for the parity 1 cows discussed previously, diagnosis of CM was assumed to occur on the median day in milk of diagnosis of all cows with that type of CM (indicated by an arrow). For several weeks prior to diagnosis, most mastitic cows had the same or slightly higher milk yield as their nonmastitic herdmates, which can be seen from the 95% CI in Table 5. This trend can also be seen in Figure 2 (A–H). However, for most pathogens, there was a sharp drop in milk production around the time of diagnosis. Then, after several weeks, milk production began to recover, and in some cases even slightly surpassed that of nonmastitic cows by the end of the follow-up period of 70 d. Hence, 305-d milk production losses will not accurately describe milk loss patterns for the different pathogens (see discussion in Gröhn et al., 1999). Results for each pathogen are given in more detail subsequently.

***Streptococcus* spp.** The milk yield of parity 2+ cows infected with *Streptococcus* spp. differed significantly from that of cows not infected with this pathogen (Table 5; Figure 2A). Before diagnosis, which occurred at a median of 80 DIM, the former cows produced significantly more milk than did the latter cows. The greatest difference occurred 3 to 4 wk prior to diagnosis when cows that would go on to develop *Streptococcus* spp. mastitis produced 3.1 kg/d more milk than their nonmastitic herdmates. But in the week before diagnosis, the opposite trend became evident. After this time, cows with CM caused by *Streptococcus* spp. produced significantly less milk than did nonmastitic cows. The worst drop in production (5.3 kg/d) occurred in the week after diagnosis. These results appear to indicate that higher producing cows may be more susceptible to infection with *Streptococcus* spp. Somatic cell count patterns of

Table 5. Effects of first occurrence of bacteria-specific clinical mastitis on milk yield in 2004 for parity 2+ cows in 2 New York State dairy farms; estimates were obtained from a mixed model with an autoregressive (Order 1) covariance structure.¹ Values are kilograms of milk/d. CI = confidence interval.

Effect	<i>Streptococcus</i> spp.		<i>Staphylococcus aureus</i>		<i>Staphylococcus</i> spp.		<i>Escherichia coli</i>		<i>Klebsiella</i> spp.		No pathogen isolated		<i>A. pyogenes</i> ³		All other pathogens	
	Est. ²	95% CI	Est.	95% CI	Est.	95% CI	Est.	95% CI	Est.	95% CI	Est.	95% CI	Est.	95% CI	Est.	95% CI
≤29 d BD ³	2.74*	1.4, 4.1	1.81	-0.1, 3.7	2.33*	0.5, 4.2	1.63*	0.5, 2.8	1.31	-0.1, 2.7	2.99*	1.8, 4.2	0.54	-1.9, 3.0	-0.60	-3.0, 1.9
22–28 d BD	3.08*	1.5, 4.7 ^a	0.61	-1.6, 2.8 ^{ab}	2.65*	0.5, 4.8 ^{ab}	2.05*	0.7, 3.4 ^{ab}	0.97	-0.7, 2.6 ^{ab}	2.83*	1.4, 4.3 ^a	-2.41	-5.7, 0.9 ^b	-1.13	-3.9, 1.6 ^{ab}
15–21 d BD	2.71*	1.0, 4.4 ^a	0.32	-2.0, 2.6 ^{ab}	2.64*	0.3, 5.0 ^a	2.42*	1.0, 3.8 ^a	1.48	-0.3, 3.2 ^a	2.53*	0.9, 4.1 ^a	-4.16*	-7.7, -0.6 ^b	-1.43	-4.4, 1.5 ^{ab}
8–14 d BD	2.16*	0.5, 3.8 ^a	0.97	-1.3, 3.3 ^a	2.43*	0.0, 4.9 ^a	2.26*	0.8, 3.7 ^a	0.80	-1.0, 2.6 ^a	2.98*	1.4, 4.6 ^a	-6.48*	-10.1, -2.8 ^b	0.76	-2.3, 3.8 ^a
1–7 d BD	-1.46	-3.2, 0.2 ^a	-0.15	-2.5, 2.2 ^a	1.98	-0.6, 4.5 ^a	0.08	-1.4, 1.6 ^a	-1.66	-3.5, 0.2 ^a	0.06	-1.6, 1.7 ^a	-7.96*	-11.2, -4.7 ^b	-0.14	-3.2, 2.9 ^a
0–7 d AD ⁴	-5.34*	-7.0, -3.7 ^a	-5.47*	-7.7, -3.3 ^a	0.19	-2.2, 2.6 ^b	-13.10*	-14.6, -11.6 ^c	-9.94*	-11.8, -8.1 ^{cd}	-5.49*	-7.1, -3.9 ^a	-12.75*	-15.6, -9.9 ^{cd}	-7.08*	-10.1, -4.0 ^{ad}
8–14 d AD	-4.06*	-5.7, -2.4 ^a	-3.65*	-6.0, -1.3 ^{ac}	1.38	-1.1, 3.9 ^b	-7.24*	-8.8, -5.7 ^{ac}	-7.79*	-9.8, -5.8 ^c	-4.07*	-5.7, -2.4 ^a	-14.19*	-17.3, -11.1 ^d	-4.45*	-7.6, -1.3 ^{ac}
15–21 d AD	-4.41*	-6.2, -2.6 ^{ad}	-3.31*	-5.7, -0.9 ^{abd}	1.16	-1.5, 3.8 ^b	-4.62*	-6.3, -3.0 ^{acd}	-6.24*	-8.4, -4.1 ^d	-2.50*	-4.2, -0.8 ^{abd}	-14.06*	-17.4, -10.7 ^e	-4.27*	-7.6, -1.0 ^{abd}
22–28 d AD	-3.76*	-5.6, -1.9 ^a	-3.59*	-6.1, -1.1 ^a	0.15	-2.6, 2.9 ^a	-4.24*	-6.0, -2.5 ^a	-4.77*	-7.0, -2.5 ^a	-2.54*	-4.3, -0.8 ^a	-13.82*	-17.3, -10.3 ^b	-1.33	-4.8, 2.1 ^a
29–35 d AD	-3.29*	-5.2, -1.4 ^a	-3.82*	-6.4, -1.2 ^a	0.82	-2.1, 3.7 ^a	-2.86*	-4.6, -1.1 ^a	-4.09*	-6.4, -1.7 ^a	-2.05*	-3.8, -0.3 ^a	-13.58*	-17.2, -9.9 ^b	-0.94	-4.5, 2.6 ^a
36–42 d AD	-2.92*	-4.8, -1.0 ^{ab}	-4.32*	-7.0, -1.6 ^a	1.79	-1.2, 4.8 ^b	-2.81*	-4.6, -1.0 ^{ab}	-3.93*	-6.3, -1.5 ^a	-1.90*	-3.7, -0.1 ^{ab}	-11.06*	-14.9, -7.2 ^c	-0.22	-3.8, 3.4 ^{ab}
43–49 d AD	-2.56*	-4.5, -0.7 ^a	-3.18*	-5.9, -0.5 ^{ab}	1.86	-1.2, 4.9 ^a	-1.80	-3.6, 0.0 ^a	-3.20*	-5.6, -0.8 ^{ab}	-1.29	-3.2, 0.6 ^a	-8.83*	-12.8, -4.8 ^b	-0.20	-3.9, 3.5 ^a
50–56 d AD	-1.76	-3.7, 0.1 ^a	-2.27	-5.0, 0.5 ^{ab}	1.04	-2.1, 4.1 ^a	-0.94	-2.8, 0.9 ^a	-2.69*	-5.1, -0.2 ^{ab}	-1.73	-3.6, 0.1 ^a	-8.79*	-12.8, -4.8 ^b	0.60	-3.1, 4.3 ^a
57–63 d AD	-2.31*	-4.1, -0.5 ^{ab}	-2.17	-4.8, 0.5 ^{ab}	-0.41	-3.5, 2.7 ^a	-1.47	-3.3, 0.3 ^a	-1.89	-4.3, 0.5 ^{ab}	-0.57	-2.4, 1.3 ^a	-7.66*	-11.5, -3.8 ^b	1.52	-2.0, 5.1 ^a
64–70 d AD	-2.17*	-3.9, -0.4 ^{ab}	-2.69*	-5.1, -0.3 ^{ab}	-1.14	-4.1, 1.8 ^{ab}	-2.12*	-3.8, -0.4 ^{ab}	-2.63*	-4.9, -0.4 ^{ab}	-0.12	-1.9, 1.7 ^a	-6.91*	-10.6, -3.3 ^b	-1.03	-4.4, 2.3 ^{ab}
≥71 d AD	-1.79*	-3.3, -0.3 ^a	-1.54	-3.6, 0.5 ^{ab}	0.14	-2.4, 2.7 ^a	-0.33	-1.8, 1.1 ^a	-1.85	-3.8, 0.1 ^{ab}	-0.05	-1.6, 1.5 ^a	-6.41*	-9.5, -3.4 ^b	0.19	-2.7, 3.1 ^a

^{a,b,c,d,e}Denote significant differences in milk loss between pathogens in a week relative to diagnosis, as measured by determining whether their 95% CI cross.

¹Other factors controlled for in the model were herd, calving season, week of lactation, and other diseases (dystocia, retained placenta, metritis, displaced abomasum, ketosis, lameness, and cystic ovary).

²Values represent the amount of milk (kg) lost (or gained) per day within the week shown, e.g., cows with *Streptococcus* spp. produced 5.3 kg less milk/d in the week immediately following diagnosis compared with cows without *Streptococcus* spp. A positive value indicates that mastitic cows produced more milk in the week than did nonmastitic cows.

³BD = Before diagnosis.

⁴AD = After diagnosis.

**P* < 0.05.

Figure 2. Lactation curves of 2 parity-2+ cows. One cow was infected with A) *Streptococcus* spp., B) *Staphylococcus aureus*, C) *Staphylococcus* spp., D) *Escherichia coli*, E) *Klebsiella* spp., F) no pathogen isolated, G) *Arcanobacterium pyogenes*, or H) all other pathogens (Panel H) (—▲—); the other cow was without the corresponding pathogen (—□—). The difference at each point of the lactation curves in each panel corresponds to the estimates in Table 5. The arrow indicates median DIM of diagnosis of the mastitic cow.

Streptococcus spp. infections also indicate a relatively severe infection, which may continue after the initial observation of CM (de Haas et al. 2002; Djabri et al. 2002).

***Staphylococcus aureus*.** The median DIM of diagnosis for *Staph. aureus* in parity 2+ cows was 93. Parity 2+ cows infected with *Staph. aureus* had a similar pattern of milk loss as those infected with *Streptococcus* spp., although their milk yield before diagnosis did not significantly differ from that of nonmastitic herdmates (Table 5; Figure 2B). The largest drop in milk, 5.5 kg/d, occurred in the week following diagnosis. *Staphylococcus aureus* was associated with reduced milk production for a prolonged period following the initial signs of CM. De Haas et al. (2002) observed that SCC was elevated even before *Staph. aureus* CM occurred, and it stayed high after its occurrence. Given the pathogenesis of *Staph. aureus* and the relatively small cure rates after treatment, this is not unexpected.

***Staphylococcus* spp.** The lactation curves for cows with and without CM caused by *Staphylococcus* spp. had a pattern apparently similar (Figure 2C). However, cows that went on to develop *Staphylococcus* spp. CM were significantly higher producers before diagnosis compared with other cows (Table 5). Cows with *Staphylococcus* spp. CM produced 2.3 to 2.7 kg/d more milk than did the latter in the month before diagnosis (Table 5). After diagnosis, occurring at a median DIM of 113, there was no statistically significant difference in milk yield between CM and nonCM cows. However, because cows with *Staphylococcus* spp. CM were higher producers before onset, they actually did suffer a large production drop in comparison with cows not infected with *Staphylococcus* spp. CM. Lam et al. (1997) studied the epidemiology of *Staphylococcus* spp. and observed a relatively small impact on SCC and CM occurrence. However, the results of the present study suggest that *Staphylococcus* spp. may be more likely to be contracted by higher producing cows, and the true milk production losses caused by *Staphylococcus* spp. may have been previously underestimated.

***Escherichia coli*.** The median day of diagnosis of *E. coli* mastitis among parity 2+ cows was 99 DIM (Figure 2D). Cows with *E. coli* produced significantly more milk prior to diagnosis than did noninfected cows, but after diagnosis, the milk production of the former group dropped off sharply (Table 5). In the first week alone, cows with *E. coli* lost 13.1 kg of milk each day. They began to recover after this, but were still producing 7.2 kg/d less milk in the second week. Losses tapered off slowly in the following weeks. Thus, *Escherichia coli* is a very important organism on dairy farms, which agrees with several studies that have previously reported the severity of *E. coli* mastitis (Montgomery et al., 1987;

Ersine et al., 1988; Hogan et al., 1989; González et al., 1990; Sears and Wilson, 2003).

***Klebsiella* spp.** For parity 2+ cows infected with *Klebsiella* spp., the median day of diagnosis was 101 (Figure 2E). *Klebsiella* spp. had no effect on milk production before diagnosis (Table 5). The largest drop in milk yield (9.9 kg/d) in cows infected with *Klebsiella* spp. occurred in the week after diagnosis. Losses became smaller, although they were still significant, in the following weeks. Based on the relatively large production losses and their persistence for a number of weeks after diagnosis, *Klebsiella* spp. appears to be a fairly important cause for concern among older dairy cows. Todhunter et al. (1991) reported on these infections and showed a relatively long duration of infection, consistent with our observation of persistent milk production loss.

“No pathogen isolated.” Parity 2+ cows that had clinical signs of mastitis but for whom a specific pathogen could not be isolated were diagnosed at a median of 87 DIM (Figure 2F). These cows produced significantly more milk before diagnosis, but for several weeks after diagnosis, they experienced significant milk loss (Table 5). For example, they produced 5.5 kg/d less milk in the first week after diagnosis than nonmastitic cows. In the second week, they produced 4.1 kg/d less milk. In subsequent weeks, the losses became smaller, and by 43 d after diagnosis, they were no longer significant. As discussed before, this type of mastitis showed similarities with gram-negative or coliform infections (González et al., 1990; Morin and Constable, 1998). In our data, a milk loss pattern very similar to *E. coli* and *Klebsiella* spp. was observed. The severity in terms of production loss was not as extreme as these confirmed gram-negative infections, possibly indicating that these were the less severe (or early cured) cases of gram-negative infections. This type of mastitis infection did not appear to be as important, in terms of production loss, as others in this study.

***Arcanobacterium pyogenes*.** Parity 2+ cows infected with *A. pyogenes* experienced very large milk losses (Table 5; Figure 2G). The median day of diagnosis was 7 DIM, quite a bit earlier than most other mastitis-causing pathogens in older cows occurring in this study. Milk loss became evident 2 to 3 wk before diagnosis, and losses grew larger in the next several weeks. The worst week, in terms of production loss, was the second week after diagnosis, when cows infected with *A. pyogenes* lost 14.2 kg/d, compared with cows not infected with this pathogen. Although milk losses decreased in subsequent weeks, cows infected with *A. pyogenes* never fully recovered; even 10 wk after diagnosis, they were still producing 6.9 kg/d less milk than their herdmates. These results indicate that *A. pyogenes* is an economi-

cally significant organism for which more research is needed regarding specific and effective control measures.

Other minor pathogens. Parity 2+ cows infected with a pathogen other than those discussed previously produced less milk than noninfected cows, only in the first 3 wk following diagnosis (Table 5; Figure 2H). Immediately after diagnosis, cows infected with one of these pathogens (see subsequent list) produced 7.1 kg/d less milk than did noninfected cows. In the second and third weeks, this loss decreased to 4.5 and 4.3 kg/d, respectively. Before diagnosis and more than three weeks after diagnosis, which occurred at a median of 81 DIM, the milk production of infected and noninfected cows did not differ significantly. The pathogens included in this category were *Pasteurella* spp., *Proteus* spp., *Serratia* spp., gram-negative *Bacillus*, yeast, gram-positive *Bacillus*, *Corynebacterium* spp., *Enterobacter* spp., and *Citrobacter* spp. As a group, they did not appear to have a long-lasting detrimental effect on milk production in older dairy cows.

Comments on Findings

Cows with CM tended to be higher producers than their nonmastitic herdmates. However, the former generally suffered a sharp drop in production, beginning even before there were any signs of mastitis. The lower production level often continued for some time, and many CM-affected cows never regained their pre-mastitic milk yield.

The point estimates in Tables 4 and 5 allow us to calculate milk losses for each pathogen studied. For example, if we assume that a primiparous cow contracts *Staph. aureus* CM on d 52 of lactation (the median DIM of diagnosis; Table 2), we can calculate the total lactational loss as follows. For the period ≥ 29 d before diagnosis, the cow actually produced 0.97 kg/d more milk than her healthy herdmates (Table 4). This value covers the period from 1 to 23 DIM ($52 \text{ d} - 29 \text{ d} = 23 \text{ d}$), and during this time, the *Staph. aureus* cow outproduced a healthy herdmate by 22.3 kg (0.97×23). Then, from 24 to 30 DIM (corresponding to 22 to 28 d before diagnosis), the *Staph. aureus* cow produced 0.94 kg/d less milk than her healthy herdmates; during that week, total loss was 6.6 kg (0.94×7). We can calculate similar losses (or gains) for each week relative to diagnosis, e.g., in the week immediately following diagnosis of *Staph. aureus*, the total loss was 58.7 kg (8.38×7). Then, for the final category (>71 d following diagnosis), if we assume a 305-d lactation, this category would include 182 d ($305 - [52 \text{ (DIM of diagnosis for this example cow)} + 71]$), and the loss for the remainder of lactation would be 325.8 kg (1.79×182). Having

completed these calculations (accounting for both losses and gains), we would discover that a primiparous cow that was diagnosed with *Staph. aureus* CM on d 52 of lactation would lose approximately 677 kg of milk over her lactation.

One must take care when performing such calculations and take into account the fact that some mastitic cows produce significantly more milk before diagnosis than their healthy herdmates; therefore, the former are actually losing even more milk than one might at first suppose. This is the case in this study with e.g., multiparous cows with *Streptococcus* spp. CM (Table 5). Before diagnosis, such cows produced 2 to 3 kg/d more milk than healthy cows. After diagnosis, they produced significantly less milk. Similarly, multiparous cows with *Staphylococcus* spp. (Table 5) significantly outproduced their healthy herdmates by approximately 2.5 kg/d before diagnosis. After diagnosis, however, it would appear that *Staphylococcus* spp. CM cows had no loss of milk yield. However, one must consider their significantly higher production before diagnosis. Only after diagnosis did they drop down to the same level as that of healthy cows. Therefore, milk loss in such cases is greater than might at first be supposed. If the cows had not contracted CM, their milk yield would have been even higher.

For other pathogens, e.g., *A. pyogenes*, milk loss began well before diagnosis and was sustained throughout lactation (Table 5).

Loss of milk yield before clinical diagnosis of mastitis in dairy cows has been previously observed (Bartlett et al., 1991; Rajala-Schultz et al., 1999b). However, it is unclear whether this loss is a subclinical effect, prediagnosis of signs, or some combination of both. This loss could be an indication of a subclinical infection before signs start, or the early stages of CM could be undetectable to the herdspersons. We are not aware of any study where cows have been cultured often enough to determine whether the drop in milk yield before CM is associated with the same agent being cultured as that found after the onset of clinical signs.

A further complication is the variability of electrical conductivity in cows' milk, so no specific threshold of it can be used to define mastitis. The electrical conductivity level of alert in the AFIKIM program depends on a 7-d rolling average of the conductivity from previous milkings. To be on the alert list, a cow must have a reading 20% above her rolling average. However, making the detection of CM even more subjective, the farm management can adjust the percentage of milk production change necessary to put a cow on the alert list: e.g., 5, 10, 20%, etc. To avoid having to look at many cows that do not have disease, the dairy can also require that 2 parameters or more be met for the cow to be

added to the alert list, e.g., both increased conductivity and decreased walking. All of these factors make detection of mastitis (whether subclinical or clinical) by use of an electrical conductivity sensor a subjective and variable process. The inclusion of a herd effect in the models helped to control for farm differences in detection of mastitis, as well as herd milk yield level.

As stated earlier, for most of the pathogens in this study, the median DIM of diagnosis of mastitis was quite a bit earlier in lactation for parity 1 cows than for older cows. This is generally due to the heifers' environment during their first 2 yr or so of life until their first calving. Parity 1 cows frequently contract mastitis, especially caused by *Streptococcus* spp. and *Staphylococcus* spp., right at their first calving (Oliver, 1987; Shearer and Harmon, 1993). Hogan et al. (1989) found that rates of coliform clinical cases were highest in the first 90 d of lactation among primiparous cows compared with multiparous cows. Matthews et al. (1992) found that the quarter prevalence of *Staphylococcus* spp. was consistently higher from parturition through the first 5 wk of lactation in primiparous cows than in multiparous cows. Just before calving, however, the quarter prevalence of *Staphylococcus* spp. was higher in multiparous cows. Thus, our findings that CM tends to occur earlier in lactation among parity 1 cows and later in lactation among parity 2+ cows for most pathogens that we studied are in broad agreement with previous studies.

One can determine the statistical significance of differences in milk loss between pathogens by comparing the 95% CI within the same time interval relative to CM diagnosis. For example, for parity 1 cows in the first week after diagnosis, the CI for *Streptococcus* spp. (−4.8 kg/d, −0.3 kg/d) and *Staph. aureus* (−11.7 kg/d, −5.1 kg/d) do not overlap, indicating that milk loss differs significantly between these two pathogens immediately after diagnosis (Table 4). Additionally, there were significant differences in milk loss between *Streptococcus* spp. and *Staph. aureus* and between *Streptococcus* spp. and “no pathogen isolated” at 8 to 14 d after diagnosis and between *Streptococcus* spp. and “no pathogen isolated” at 57 to 63 d and ≥71 d after diagnosis in parity 1 cows. These differences are indicated by different superscripts in the relevant rows (i.e., weeks relative to CM diagnosis) of Table 4.

Many more differences in 95% CI were observed for older cows (Table 5). In the first several weeks following CM diagnosis, there were significant differences in milk loss among most pairs of pathogens. Milk loss caused by *A. pyogenes* was significantly greater than that caused by most other pathogens in most weeks, both before and after diagnosis. In the first week after diagnosis, milk loss caused by *Staphylococcus* spp. was sig-

nificantly less than that caused by any other pathogen. In contrast, in this week, milk loss caused by *E. coli* was significantly greater than that caused by *Streptococcus* spp., *Staph. aureus*, “no pathogen isolated,” and “all other pathogens.” Similarly, milk loss caused by *Klebsiella* spp. was significantly greater than that caused by *Streptococcus* spp., *Staph. aureus*, and “no pathogen isolated” in the first week after diagnosis. As in the preceding week, milk loss caused by *Staphylococcus* spp. in the second week after diagnosis was significantly less than that of any other pathogen. Milk loss caused by *Klebsiella* spp. was significantly greater than that caused by *Streptococcus* spp. and “no pathogen isolated” in the second week following diagnosis. In the third week (15 to 21 d) after diagnosis, milk loss caused by *Staphylococcus* spp. was significantly less than that caused by *Streptococcus* spp., *E. coli*, and *Klebsiella* spp. In addition, from 36 to 42 d after diagnosis, milk loss caused by *Staph. aureus* and *Klebsiella* spp. was significantly greater than that caused by *Staphylococcus* spp. Milk loss caused by *A. pyogenes* was significantly greater than that caused by *Streptococcus* spp., *Staphylococcus* spp., *E. coli*, “no pathogen isolated,” and “all other pathogens” more than 70 d following diagnosis.

These findings demonstrate that milk loss varies with different CM-causing pathogens, depending on time relative to diagnosis. The largest number of differences was found immediately following diagnosis. There was more variation between pathogens in multiparous cows than in primiparous cows.

CONCLUSIONS

Milk loss caused by pathogen-specific CM has not been studied previously using all of the methods combined here. This paper has addressed this question in detail, using weekly milk weights (i.e., mean daily yield in each week) and state of the art statistical methodology (mixed models with an autoregressive covariance structure). The results indicate that milk loss in mastitic cows did indeed vary depending on the pathogen responsible for the mastitis. Among parity 1 cows, *Staph. aureus*, *E. coli*, and *Klebsiella* spp. caused the greatest declines in milk yield. Milk yield also dropped in clinically mastitic cows for whom no pathogen was isolated. Among mastitic parity 2+ cows, *Streptococcus* spp., *Staph. aureus*, *E. coli*, *Klebsiella* spp., and *A. pyogenes* were responsible for the largest milk losses. In general, in both groups of cows, milk yield often began to drop several weeks before diagnosis of CM. The milk losses were greatest soon after diagnosis and then generally tapered off in subsequent weeks. For some pathogens, milk losses persisted long after diagnosis. These findings have implications for determining the profit-

ability of cows suffering from CM. On the one hand, cows with CM tended to be higher producers than their nonmastitic herdmates. However, the former generally suffered a sharp drop in production, beginning even before there were any signs of mastitis. The lower production level often continued for some time, and many CM-affected cows never regained their premastitic milk yield. This study should be of interest to dairy producers to determine which specific mastitic pathogens are most detrimental to their cows' well-being, production, and profitability and when in lactation the pathogens' effects occur.

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