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# Associations of the first occurrence of pathogen-specific clinical mastitis with milk yield and milk composition in dairy cows

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The aim of this study was to estimate the associations of the first occurrence of pathogen-specific clinical mastitis (CM) with milk yield and milk composition (somatic cell count (SCC), lactose, fat, protein content in milk and milk urea nitrogen (MUN)). We studied 3149 dairy cows in 31 Hokkaido dairy farms in Japan. Five pathogen groups were studied: *Streptococcus* spp.; *Staphylococcus aureus* (*S. aureus*); coagulase-negative staphylococci (CNS); coliforms; and fungi. Test-day milk data and clinical records were collected from June 2011 until February 2014. Mixed models with an autoregressive correlation structure were fitted to quantify the effects of CM and several other control variables (herd, calving season, parity, week of lactation, and other diseases). Primipara (first lactation) and multipara (second and later lactations) were analysed separately. All pathogens, particularly *S. aureus* and fungi, were associated with significant milk losses in multipara. In this study, *S. aureus* and CNS infections were not associated with significant milk loss in primipara. All pathogens, in particular *S. aureus* and fungi, significantly increased SCC in both parity groups. All pathogens, especially CNS (in primipara) and *S. aureus* (in multipara), decreased lactose content. All pathogen groups except for fungi were associated with significant changes in fat, protein and MUN. Some pathogens such as *Streptococcus* spp. and coliforms seemed to be associated with long-term fat, protein and MUN changes. These findings provide estimates that could be used to calculate precise costs of CM, and also provide better indicators of pathogen-specific mastitis.

**Keywords:** Milk yield, milk composition, SCC, mastitis, pathogen.

Mastitis, an intramammary inflammation, is a common and costly disease in many dairy herds around the world (e.g. Sears & Wilson 2003; Halasa et al. 2007). Mastitic dairy cows experience milk loss (Houben et al. 1993; Gröhn et al. 2004) and poor quality of milk (Kitchen, 1981; Coulon et al. 2002). Milk loss is a large component of the cost of mastitis. Poor quality of milk, as exemplified by high somatic cell count (SCC) and compositional change in milk, can be detrimental to profitability because it may decrease milk price. It is critical for the dairy industry, especially for cheese production and quality (Leitner et al. 2006; Blum et al. 2014).

Somatic cell count in milk is a parameter of great economic importance in dairy herds. A high SCC is usually indicative of a response to an intramammary infection (Harmon, 1994; Schukken et al. 2011). Many studies have reported high SCC for mastitic cows (e.g. Coulon et al. 2002; Leitner et al. 2006; Jamrozik & Schaeffer, 2012). Other parameters for milk quality include lactose, fat and protein contents in milk. These may affect milk pricing and are important in the dairy industry. Mastitis seems to reduce lactose content (Coulon et al. 2002; Bezman et al. 2015) but has little or no effect on protein and fat content

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(Botaro et al. 2015; Kester et al. 2015; Tomazi et al. 2015). However, it is not prudent to consider these changes in milk without pathogen information and precise cow information including parity and days in milk (DIM), since the change in milk due to mastitis might be pathogen-specific (e.g. Coulon et al. 2002; Bezman et al. 2015), and parity- and DIM-dependent (Stanton et al. 1992; de Haas et al. 2002, 2004; Jensen et al. 2016).

In this study, our objective was to estimate the parity- and DIM-dependent associations of the first occurrence of pathogen-specific clinical mastitis (CM) with milk yield and milk composition in dairy cows. Five pathogen groups were studied: *Streptococcus* spp.; *Staphylococcus aureus* (*S. aureus*); coagulase-negative staphylococci (CNS); coliforms; and fungi (mainly yeast like). Use of mixed models enabled us to study (1) how much milk yield and milk composition change due to pathogen-specific CM, and (2) when the milk losses and compositional changes start and end in the lactation. The models provide estimates that can be used to calculate precise costs of CM, and provide better indicators of mastitis that could be useful for earlier and automatic detection of infection and more timely treatment of infected cows.

## Materials and methods

### *Herd descriptions*

Thirty-one Holstein herds, from Obihiro City in Hokkaido, Japan, participated in the study. Average herd size was 54 milking cows (range: 32 to 107 cows) with an average 305-d milk yield of 9187 kg/cow (range: 7107 to 11 956 kg/cow), and monthly mean SCC across the population of the tested cows of 197 200 (range: 96 991 to 299 053) cells/mL. Data on milk production, milk composition, parity, reproductive performance, diseases, calving, drying-off, and culling were collected from June 2011 until February 2014. Most cows (21 herds) were housed in tie stalls, and the others (10 herds) were housed in free stalls in covered barns. They were fed either total mixed ration (TMR) or by separate feeding. Most of them were milked twice a day.

### *Data collection*

The test-day data of milk yield and milk composition, and medical records, were obtained from the Obihiro Husbandry Center and Tokachi Agricultural Insurance Association, respectively. The test-day milk data were collected monthly in each farm. The test-day milk yield was estimated from single milkings (alternate (AT) method, Smith & Pearson, 1981) in 25 herds or directly measured from evening-morning samples in 6 herds. Milk sampled by staff in the Obihiro Husbandry Center was carried in a box containing refrigerant and artificial preservatives to the Milk Testing Laboratory in Obihiro City in Hokkaido, Japan. FOSS MilkoScan™ FT+ was used to measure milk composition including SCC, concentration of milk fat, protein, lactose, solids-not-fat (SNF) and milk urea nitrogen (MUN), using milk samples heated at 40 °C (range: 38–42 °C). Solids-not-fat was excluded from the analysis, since it included protein content.

### *Case definitions*

Fourteen veterinarians identified the CM cases, according to their prescription for diagnosis, characterised by changes in milk consistency or hard swollen udder. All CM cases were diagnosed by veterinarians' clinical examination and microbial culture based on requests from dairy farmers. In order to identify pathogens, milking samples were first collected by farmers according to the prescription: (1) scrub teat ends with alcohol swab, (2) discard a few streams of milk from the teat and (3) collect milk sample in a sterile tube. The milk samples were then refrigerated at 4 °C, sent to a laboratory for analysis, plated on 5% sheep blood agar and incubated aerobically overnight at 37 °C. Identification of isolates was according to Gram staining. If it was impossible to identify isolates, additional biochemical tests, such as the catalase test and cytochrome-oxidase test, were performed. Antibiotic susceptibility tests were performed to select the most appropriate antimicrobial agent as necessary. If 2 different pathogens (e.g. *Streptococcus* spp. and coliforms) were isolated on the same day, the veterinarian determined which pathogen would contribute to the analysis, based on bacterial counts. This study focused on CM cases that occurred on DIM $\leq$ 365. Repeated CM cases of any pathogen (e.g. *Strep.* spp. then some other pathogen), which were incorporated into the mixed model in order to exclude their effects on the changes in milk after the first CM cases, were assumed to occur $\geq$14 d after the previous CM (Barkema et al. 1998; Hertl et al. 2011). Any CM case occurring <14 d after the previous case (of the same pathogen) was considered to be the same case.

The other 4 diseases (displaced abomasum (DA), milk fever, puerperal fever and ketosis), which were diagnosed and treated by veterinarians, were included in the model as potential confounders. This study focused on the cases of DA, milk fever, puerperal fever and ketosis that occurred on DIM $\leq$ 365.

### *Statistical analysis*

The 43 149 test-day records (primipara: 13 054, multipara: 30 095) of milk yield and composition, from 3149 cows (primipara: 1763 and multipara: 2422; a cow can belong in both classes) with 5996 lactations (primipara: 1763 and multipara: 4233), were analysed. All records for cows that experienced mastitis before the first calving were excluded from the dataset. Also, all records for 8$^{th}$ and higher lactations were excluded from the dataset.

The associations of the first occurrence of pathogen–specific CM with weekly milk yield and milk composition for

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that same week (week in milk, WIM) were studied using monthly test-day milk data. Estimation of weekly milk production and composition from the many monthly test-day milk data was possible, since each cow had different WIM on the test day. Other control variables in the model were herd, parity, calving season, WIM, and the other four diseases. The R procedure, lme (R version 3.1·2, 2014), was used to fit mixed models. Herd was modelled as a random (intercept) effect. The other variables were modelled as fixed effects. A first-order autoregressive correlation structure among the repeated measurements of milk yield and composition within a cow's lactation was incorporated. These models were adopted from earlier research on the effects of pathogen-unidentified or -specific CM on milk yield (Gröhn et al. 2004; Wilson et al. 2004; Bar et al. 2007; Hertl et al. 2014). Wilson et al. (2004) showed a first-order autoregressive correlation structure among the repeated measurements of milk yield was the best structure in their analyses.

Parity groups (first ('parity 1'), and second and greater ('parity ≥2')) were analysed separately. For parity ≥2 cows, the following mixed model with a correlated error term, represented by e, was used for study of pathogen-specific CM:

$$\begin{aligned} Y = {} & \text{parity (6 index variables)} \\ & + \text{calving season (4 index variables)} \\ & + \text{WIM (44 index variables)} + \text{DA (6 index variables)} \\ & + \text{milkfever (6 index variables)} \\ & + \text{puerperal fever(6 index variables)} \\ & + \text{ketosis (6 index variables)} \\ & + \textit{Streptococcus} \text{ spp. (8 index variables)} \\ & + \textit{S.aureus} \text{ (8 index variables)} + \text{CNS (8 index variables)} \\ & + \text{Coliforms (8 index variables)} + \text{Fungi (8 index variables)} \\ & + \text{others (8 index variables)} + \text{herd(random)} + \text{e}, \end{aligned}$$

where $Y$ is test-day milk yield or composition. Separate models were fit for each $Y$ (i.e. milk yield or each composition (SCC, lactose, fat, protein content in milk, MUN)). Within the older group of parity ≥2 cows, parity was subdivided into 6 categories of parity 2, 3, 4, 5, 6, and 7. Calving season had 4 categories: March through May, June through August, September through November, and December through February. WIM was modelled as an index variable, representing 44 levels for the first 44 week of lactation, which covers 305 d of lactation. For each disease, an index variable was created to classify the milk yield and composition according to when they were measured in relation to disease occurrence. For each mastitis pathogen, an index variable was created with 7 levels: ≥29, 15–28, 1–14 d before diagnosis, the same day (0)–13, 14–27, ≥28 d after diagnosis without any more cases of CM and ≥28 d after diagnosis and experienced second and more cases of CM. This index enabled us to precisely determine when mastitis affected milk yield and composition, even before diagnosis. Each of the other diseases (DA, milk fever, puerperal fever and ketosis) was modelled with 6 levels: before diagnosis, same day (0)–14, 15–28, 29–42, 43–56, and ≥57 d after diagnosis. These other diseases occurred very early in lactation. For primipara (parity1), the above model excluding the parity term was fit.

## Results

### *Descriptive findings*

Table 1 presents the lactational incidence risk, number, median and mean DIM (and range) of clinical cases in the 31 Hokkaido dairy herds in Japan by parity group (1, and ≥2) and for each pathogen studied. *Streptococcus* spp. and coliforms were two of the most commonly isolated pathogens, followed by CNS. For most pathogens except fungi, the incidence of CM was higher among older cows than those in parity 1. Cases of CM occurred throughout lactation. The median day of lactation for diagnosis of most cases occurred in midlactation. Cases of CM by fungi tended to occur later than the other pathogens. Most of these findings, except for CNS and fungi, are in line with previous studies (e.g. Gröhn et al. 2004). Descriptive findings for repeated CM cases of any pathogen are shown in the online Supplementary file, and Supplementary Table S1 shows the lactational incidence risk of the other diseases controlled for in the models estimating milk loss and compositional change in milk.

### *Milk losses and compositional changes*

Figures 1–6 present estimated milk losses and compositional changes associated with the first occurrence of each CM pathogen in each parity group (1 and ≥2), assumed calved in mid spring and the random effect for herds was averaged. The results of each component (milk yield or composition) in each parity group were estimated by a model in this study that included all pathogens simultaneously, and by using monthly milk yield and milk composition of non-mastitic and mastitic cows. For the mastitic cow, diagnosis of CM was assumed to occur on the median DIM of diagnosis of all cows with that pathogen-specific CM (indicated by an arrow). The difference at each point of the curves in each panel corresponds to the estimates in online Supplementary Tables S2 and S3.

Our findings are summarised below and detailed descriptions of the results are presented in the Supplementary File. The associations of non-CM diseases (DA, milk fever, puerperal fever and ketosis) with milk yield and milk composition are presented in Supplementary Tables S4 and S5.

All pathogens were associated with significant milk losses for at least 2 weeks after the diagnosis, particularly in older cows (Fig. 1). The estimation showed that higher yielding (particularly older) cows were at greater risk for the infection, as Gröhn et al. 2004 have previously reported. Key

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**Table 1.** Lactational incidence risk (number of clinical cases) and median and mean days in milk (and range) of the first occurrence of pathogen-specific clinical mastitis by parity group in 31 Hokkaido dairy herds in Japan

| Parity† | Total | Pathogen | | | | | |
|---|---|---|---|---|---|---|---|
| | | *Streptococcus* spp. | *S. aureus* | CNS | Coliforms | Fungi | Others‡ |
| | Lactational incidence risk (number of clinical cases) | | | | | | |
| 1 | 21·8% (385) | 6·0% (105) | 1·2% (22) | 2·0% (35) | 4·9% (86) | 0·9% (16) | 6·9% (121) |
| ≥2 | 32·8% (1388) | 6·9% (293) | 1·7% (72) | 3·4% (142) | 7·5% (318) | 0·8% (33) | 12·5% (530) |
| | Median; mean days in milk (range) | | | | | | |
| 1 | 88; 109 (1–365) | 71; 90 (1–353) | 66; 79 (3–205) | 99; 126 (2–349) | 79; 93 (1–319) | 126; 163 (38–362) | 122; 131 (1–365) |
| ≥2 | 85; 106 (1–365) | 88; 109 (1–352) | 91; 114 (1–357) | 103; 109 (1–342) | 72; 95 (1–351) | 39; 71 (1–240) | 91; 112 (1–365) |

†Parity 1 ($n = 1763$), Parity ≥2 ($n = 4233$)
‡'Others' group includes the cases in which (1) pathogens were not identified (main cases in this group), (2) other minor pathogens such as *Pseudomonas aeruginosa* and *Trueperella pyogenes*, which caused only a few cases of CM in this study, were identified, and (3) 3 or more different pathogens were isolated on the same day

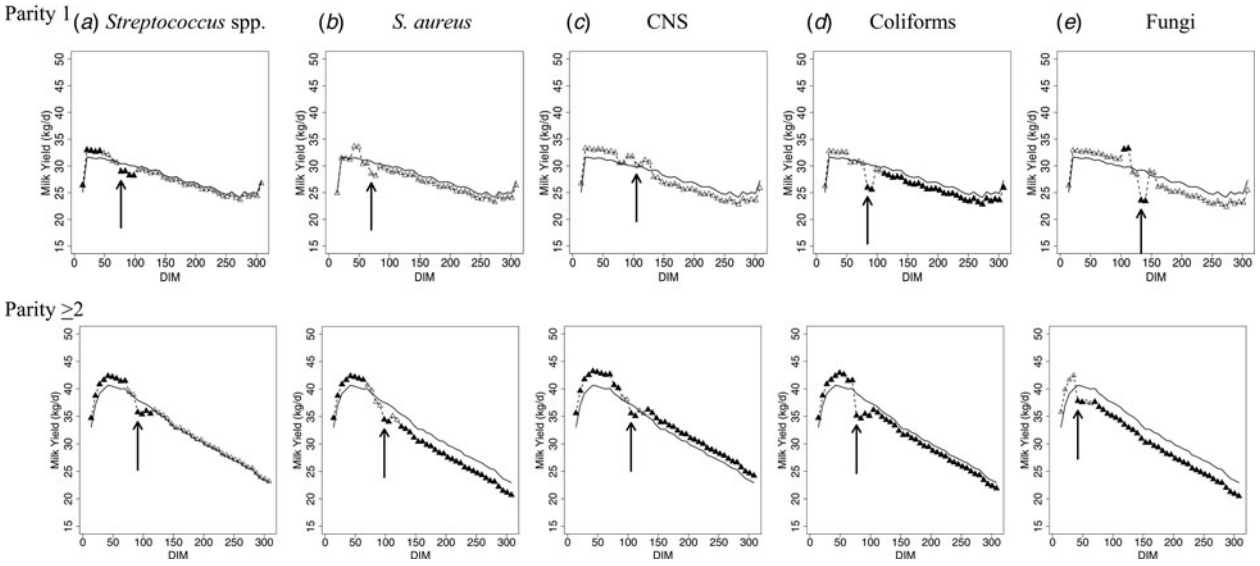


**Fig. 1.** Estimated lactation curves from 1763 parity 1 and 2422 parity ≥2 cows, respectively. Each curve is for a mastitic cow (- -Δ- -) infected with each pathogen (in separate panels) and for a non-mastitic cow ( —— ). The significant change is represented by (- -▲- -, black triangle). The arrow indicates median DIM of diagnosis of the mastitic cow.

findings from our study regarding milk losses, in older cows, are (1) the greatest and longest-term milk losses were caused by *S. aureus* and fungi and (2) recovery of potential milk production in CNS-infected cows and mild recovery in *Streptococcus* spp.-infected cows. (3) Only coliforms caused significant long-term milk losses, and *S. aureus* and CNS infections did not show any significant milk losses, in younger cows.

All pathogens, in particular *S. aureus* and fungi, significantly increased SCC from at least 2 weeks before the diagnosis until 2 weeks–1 month after the diagnosis in both parity groups (Fig. 2). *Staphylococcus aureus* was associated with significantly high SCC throughout the lactation even before the diagnosis (from just after calving; this might imply subclinical infection due to *S. aureus*). In younger cows, the peak SCC level due to *S. aureus* or fungi infection reached over 500 000–1 000 000 cells/mL. The highest peak SCC level due to coliforms infection reached over 500 000 cells/mL in older cows.

All pathogens, particularly CNS, *S. aureus,* and also coliforms and fungi, decreased lactose content for 2 weeks–1 month after diagnosis and, sometimes, throughout the lactation. Effects of CNS or *S. aureus* infections on lactose decline were different between younger and older cows (Fig. 3). All pathogen groups were associated with significant changes in fat (Fig. 4), and all pathogen groups except for fungi were associated with significant changes in protein (Fig. 5). *Streptococcus* spp., coliforms and *S. aureus* infections were associated with significantly low MUN (Fig. 6). Some pathogens such as *Streptococcus* spp. and coliforms seemed to be associated with long-term fat, protein and MUN changes.

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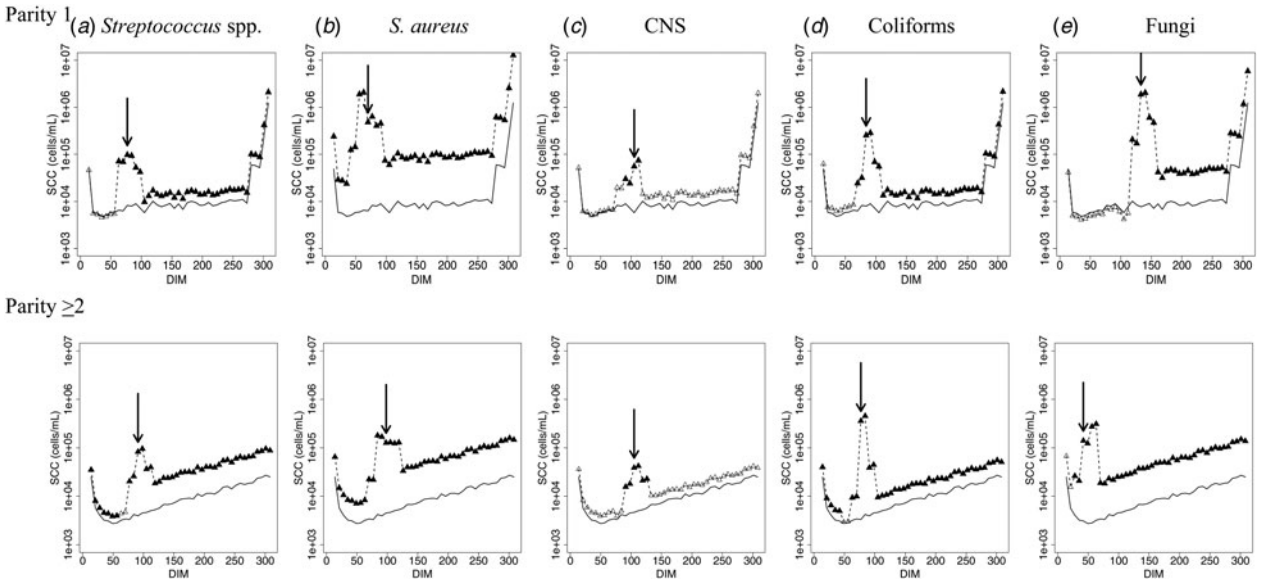


**Fig. 2.** Estimated somatic cell count (SCC) curves from 1763 parity 1 and 2422 parity ≥2 cows, respectively. Each curve is for a mastitic cow (- -Δ- -) infected with each pathogen (in separate panels) and for a non-mastitic cow ( —— ). The significant change is represented by (- -▲- -, black triangle). The arrow indicates median DIM of diagnosis of the mastitic cow.

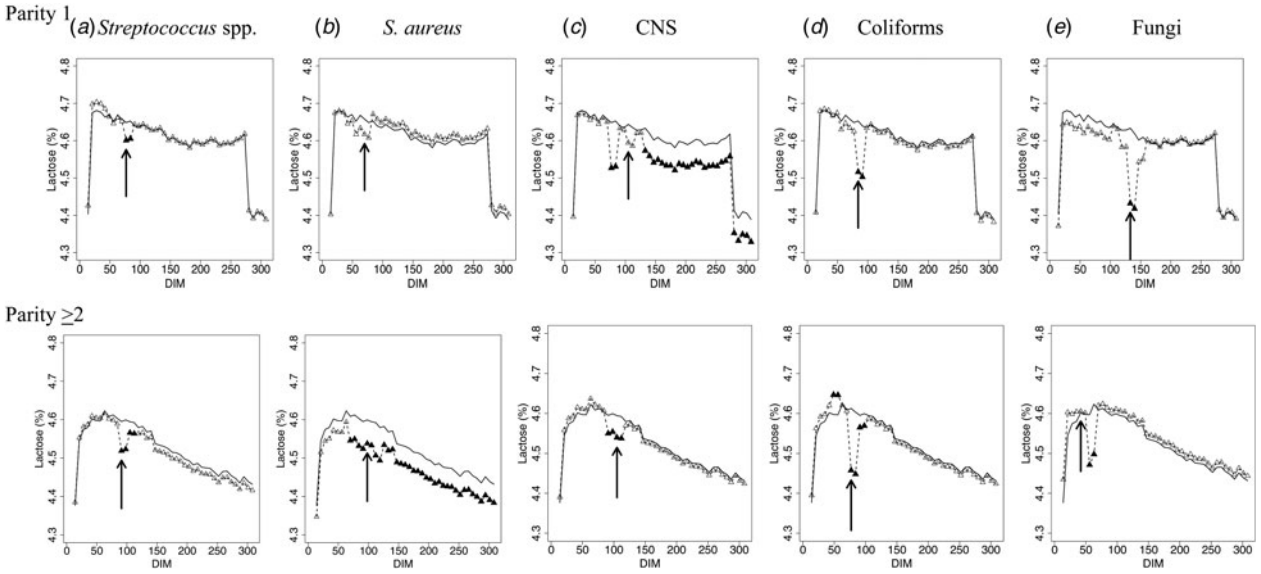


**Fig. 3.** Estimated lactose curves from 1763 parity 1 and 2422 parity ≥2 cows, respectively. Each curve is for a mastitic cow (- -Δ- -) infected with each pathogen (in separate panels) and for a non-mastitic cow ( —— ). The significant change is represented by (- -▲- -, black triangle). The arrow indicates median DIM of diagnosis of the mastitic cow.

## Discussion

### *Classification of the infections (pathogens) based on milk*

*Staphylococcus aureus* and fungi were associated with the most significant milk losses in older cows and high SCC content in both parity groups. These highlight the severity of *S. aureus* and fungi infections, although they are not the most common pathogens (their lactational incidence risk was 1–2%, Table 1). Also, the high SCC level of older cows that became infected by *S. aureus* implies that they may be subclinically infected. Interestingly, in younger cows, these pathogens did not cause large milk losses (only temporary losses by fungi infection). This does not imply mildness of the infections, but the immune system of younger cows might overcome the infections due to *S. aureus* and fungi. Also, *S. aureus* might not cause significant damage to the mammary gland of younger cows (since lactose contents did not decrease due to the infection) but

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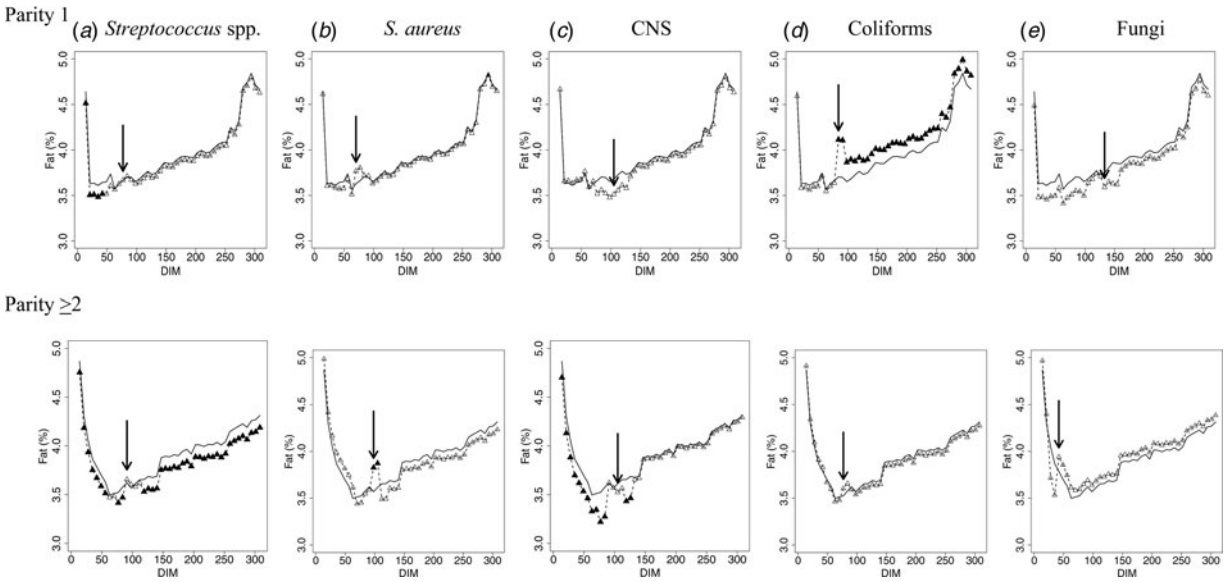


**Fig. 4.** Estimated fat curves from 1763 parity 1 and 2422 parity ≥2 cows, respectively. Each curve is for a mastitic cow (- -Δ- -) infected with each pathogen (in separate panels) and for a non-mastitic cow ( —— ). The significant change is represented by (- -▲- -, black triangle). The arrow indicates median DIM of diagnosis of the mastitic cow.

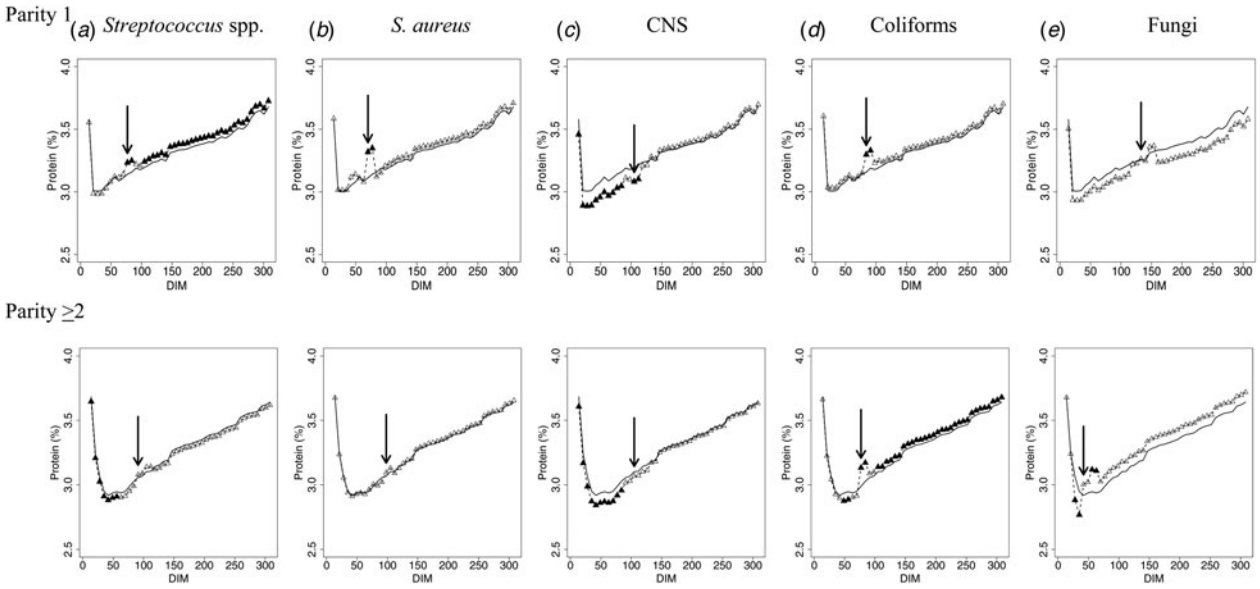


**Fig. 5.** Estimated protein curves from 1763 parity 1 and 2422 parity ≥2 cows, respectively. Each curve is for a mastitic cow (- -Δ- -) infected with each pathogen (in separate panels) and for a non-mastitic cow ( —— ). The significant change is represented by (- -▲- -, black triangle). The arrow indicates median DIM of diagnosis of the mastitic cow.

might cause significant damage to the mammary gland of older cows (since persistent low lactose contents due to the infection were estimated), where the damage to the mammary gland might be functional and/or structural (related to tight junction status). It might be possible to automatically detect *S. aureus* infections based on (1) higher SCC level even in early lactation in both parity groups, (2) persistent low lactose content, (3) temporary high fat content and (4) low MUN, in older cows. Fungi infections may be detected by high SCC level and low lactose content. A high SCC level, over 500 000–1 000 000 cells/mL in younger cows, might imply *S. aureus* or fungi infection.

Coliforms caused long-term milk losses, as previous works have shown (Gröhn et al. 2004; Bezman et al. 2015). In this study, the lactational incidence risks were 4·9% in primipara and 7·5% (the highest) in multipara.

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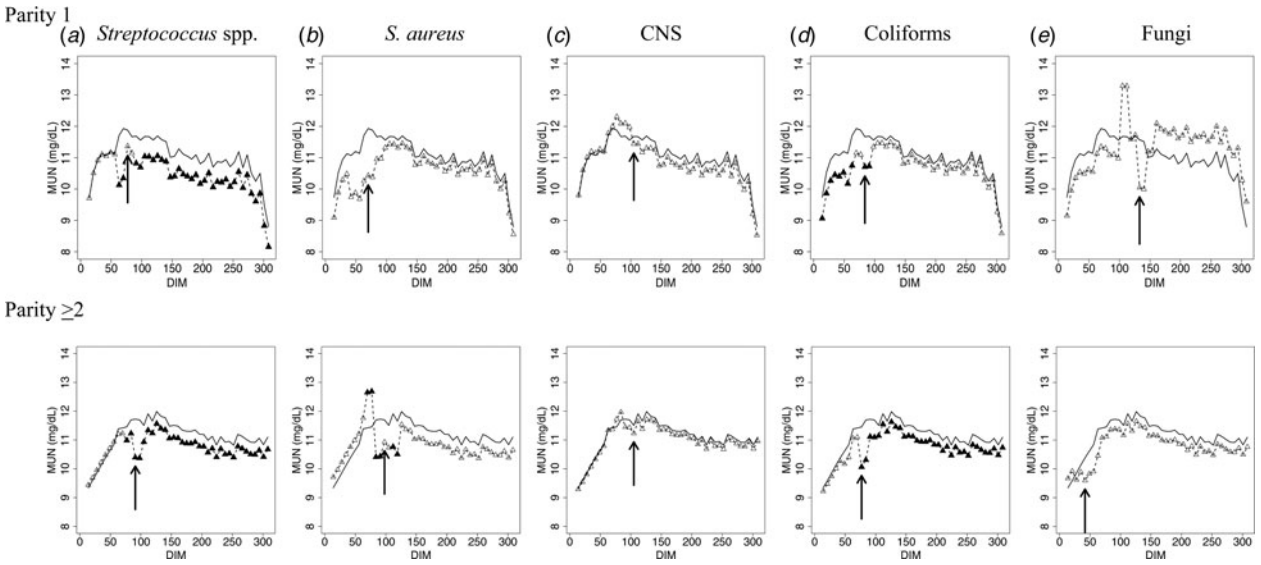


**Fig. 6.** Estimated milk urea nitrogen (MUN) curves from 1763 parity 1 and 2422 parity ≥2 cows, respectively. Each curve is for a mastitic cow (- -Δ- -) infected with each pathogen (in separate panels) and for a non-mastitic cow ( —— ). The significant change is represented by (- -▲- -, black triangle). The arrow indicates median DIM of diagnosis of the mastitic cow.

Coliforms infections may specifically be detected by (1) high fat content in younger cows and (2) high protein content in both parity groups, while such infections also caused high SCC levels (particularly in older cows), low lactose content, and low MUN.

*Streptococcus* spp. infections also caused milk losses. Their lactational incidence risk was high (6–7%, Table 1). Specific compositional changes associated with *Streptococcus* spp. infections were (1) persistent low fat content in older cows, (2) persistent high protein content in younger cows, and (3) persistent low MUN in both parity groups.

CNS did not show persistent milk losses in either parity group, implying mildness of the infection. However, the lactational incidence risk was relatively high (2–3%, Table 1), and it might be very important to distinguish CNS infections from other infections. Specific compositional changes in CNS infections were (1) persistent low lactose in younger cows, (2) low fat content before diagnosis in older cows, and (3) low protein content before diagnosis in both parity groups. The persistent low lactose in younger cows, not in older cows, might reflect persistent damage to their mammary gland due to weakness of the younger cows (such as a defective immune system). The low protein content before diagnosis might reflect insufficient energy intake that may cause vulnerability to CNS infections. These CNS-specific changes in milk might be helpful to distinguish CNS infections from other infections.

### *Comments on the changes in milk*

Milk losses due to CM have been well studied even as pathogen-specific and parity-and DIM-dependent (e.g., Gröhn et al. 2004). The high SCC content due to mastitis is also well studied, even as pathogen-specific and DIM-dependent, but not parity-specific and not including fungi (e.g. de Haas et al. 2002 and 2004), although Green et al. (2004) have reported SCC distributions during lactation for the prediction of CM.

Previous studies reported lactose decline due to pathogen-specific CM, but not parity- and DIM-dependent. Coulon et al. (2002), Leitner et al. (2006), Bezman et al. (2015) and Kester et al. (2015) showed lower lactose contents in milk caused by *S. aureus*, *E. coli*, some species of *Streptococcus* and CNS, although some of these works did not provide parity information, and Botaro et al. (2015) reported no significant lactose change by *S. aureus* for subclinical cases.

Clinical mastitis might be associated with fat, protein and MUN changes in milk. Previous works regarding fat and protein changes due to CM, although some of them were not pathogen-specific and DIM- and parity-dependent, showed high fat and low protein contents (Coulon et al. 2002; Jamrozik & Schaeffer, 2012) and, conversely, low fat contents due to *Streptococcus* spp. infections (Bezman et al. 2015). Other studies noted no significant change in fat and protein content due to mastitis (Botaro et al. 2015; Tomazi et al. 2015). The association of CM and MUN has not been focused on, but it might be worth further study, particularly for *Streptococcus* spp. and coliforms infections.

Our findings regarding milk losses and compositional changes can provide parity- and DIM-dependent parameter estimates which can be used to obtain precise cost estimation and better indicators of pathogen-specific CM.

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## Supplementary material

The supplementary material for this article can be found at https://doi.org/10.1017/S0022029918000456.

This study used the dataset of the herd tests and medical records given by the Obihiro Husbandry Center and Tokachi Agricultural Insurance Association. The authors are grateful to Akihiro Kamikawa for helpful discussion related to the mammary gland and milk composition.

## References

**Bar D, Gröhn YT, Bennett G, González RN, Hertl JA, Schulte HF, Tauer LW, Welcome FL & Schukken YH** 2007 Effect of repeated episodes of generic clinical mastitis on milk yield in dairy cows. *Journal of Dairy Science* **90** 4643–4653

**Barkema HW, Schukken YH, Lam TJ, Beiboer ML, Wilmink H, Benedictus G & Brand A** 1998 Incidence of clinical mastitis in dairy herds grouped in three categories by bulk milk somatic cell counts. *Journal of Dairy Science* **81** 411–419

**Bezman D, Lemberskiy-Kuzin L, Katz G, Merin U & Leitner G** 2015 Influence of intramammary infection of a single gland in dairy cows on the cow's milk quality. *Journal of Dairy Research* **82** 304–311

**Blum SE, Heller ED & Leitner G** 2014. Long term effects of *Escherichia coli* mastitis. *Veterinary Journal* **201** 72–77

**Botaro BG, Cortinhas CS, Dibbern AG, Silva LFP, Benites NR & dos Santos MV** 2015. *Staphylococcus aureus* intramammary infection affects milk yield and SCC of dairy cows. *Tropical Animal Health Production* **47** 61–66

**Coulon JB, Gasqui P, Barnouin J, Ollier A, Pradel P & Promiès D** 2002. Effect of mastitis and related-germ on milk yield and composition during naturally-occurring udder infections in dairy cows. *Animal Research* **51** 383–393

**de Haas Y, Barkema HW, & Veerkamp RF** 2002. The effect of pathogen-specific clinical mastitis on the lactation curve for somatic cell count. *Journal of Dairy Science* **85** 1314–1323

**de Haas Y, Veerkamp RF, Barkema HW, Gröhn YT & Schukken YH** 2004 Associations between pathogen-specific cases of clinical mastitis and somatic cell count patterns. *Journal of Dairy Science* **87** 95–105

**Green MJ, Green LE, Schukken YH, Bradley AJ, Peeler EJ, Barkema HW, & Medley GF** 2004 Somatic cell count distributions during lactation predict clinical mastitis. *Journal of Dairy Science* **87** 1256–1264

**Gröhn YT, Wilson DJ, González RN, Hertl JA, Schulte H, Bennett G & Schukken YH** 2004. Effect of pathogen-specific clinical mastitis on milk yield in dairy cows. *Journal of Dairy Science* **87** 3358–3374

**Halasa T, Huijps K, Østerås O & Hogeveen H** 2007 Economic effects of bovine mastitis and mastitis management: A review. *Veterinary Quarterly* **29** 18–31

**Harmon RJ** 1994 Physiology of mastitis and factors affecting somatic cell counts. *Journal of Dairy Science* **77** 2103–2112

**Hertl JA, Schukken YH, Bar D, Bennett GJ, González RN, Rauch BJ, Welcome FL, Tauer LW & Gröhn YT** 2011 The effect of recurrent episodes of clinical mastitis caused by Gram-positive and Gram-negative bacteria and other organisms on mortality and culling in Holstein dairy cows. *Journal of Dairy Science* **94** 4863–4877

**Hertl JA, Schukken YH, Welcome FL, Tauer LW & Gröhn YT** 2014 Pathogen-specific effects on milk yield in repeated clinical mastitis episodes in Holstein dairy cows. *Journal of Dairy Science* **97** 1465–1480

**Houben EHP, Dijkhuizen AA, van Arendonk JAM & Huirne R** 1993 Short- and long-term production losses and repeatability of clinical mastitis in dairy cattle. *Journal of Dairy Science* **76** 2561–2578

**Jamrozik J & Schaeffer LR** 2012 Test-day somatic cell score, fat-to-protein ratio and milk yield as indicator traits for sub-clinical mastitis in dairy cattle. *Journal of Animal Breeding and Genetics* **129** 11–19

**Jensen DB, Hogeveen H & De Vries A** 2016 Bayesian integration of sensor information and a multivariate dynamic linear model for prediction of dairy cow mastitis. *Journal of Dairy Science* **99** 7344–7361

**Kester HJ, Sorter DE & Hogan JS** 2015 Activity and milk compositional changes following experimentally induced *Streptococcus uberis* bovine mastitis. *Journal of Dairy Science* **98** 999–1004

**Kitchen BJ** 1981 Bovine mastitis: milk compositional changes and related diagnostic tests. *Journal of Dairy Research* **48** 167–188

**Leitner G, Krifucks O, Merin U, Lavi Y & Silanikove N** 2006 Interactions between bacteria type, proteolysis of casein and physico-chemical properties of bovine milk. *International Dairy Journal* **16** 648–654

**Schukken YH, Günther J, Fitzpatrick J, Fontaine MC, Goetze L, Holst O, Leigh J, Petzl W, Schuberth HJ, Sipka A, Smith DG, Quesnell R, Watts J, Yancey R, Zerbe H, Gurjar A, Zadoks RN, Seyfert HM** & members of the Pfizer mastitis research consortium 2011 Host-response patterns of intramammary infections in dairy cows. Veterinary Immunology and Immunopathology 144 270–289

**Sears PM & Wilson DJ** ed. 2003 Mastitis. *Veterinary Clinics North America: Food Animal Practice* **19** 1–265

**Smith JW & Pearson RE** 1981 Development and evaluation of alternate testing procedures for official records. *Journal of Dairy Science* **64** 466–474

**Stanton TL, Jones LR, Everett RW & Kachman SD** 1992 Estimating milk, fat, and protein lactation curves with a test day model. *Journal of Dairy Science* **75** 1691–1700

**Tomazi T, Gonçalves JL, Barreiro JR, Arcari MA & dos Santos MV** 2015 Bovine subclinical intramammary infection caused by coagulase-negative staphylococci increases somatic cell count but has no effect on milk yield or composition. *Journal of Dairy Science* **98** 3071–3078

**Wilson DJ, González RN, Hertl JA, Schulte H, Bennett G, Schukken YH & Gröhn YT** 2004. Effect of clinical mastitis on the lactation curve: a mixed model estimation using daily milk weights. *Journal of Dairy Science* **87** 2073–2084

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