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# Genetic associations for pathogen-specific clinical mastitis and patterns of peaks in somatic cell count

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## Abstract

*Genetic associations were estimated between pathogen-specific cases of clinical mastitis (CM), lactational average somatic cell score (LACSCS), and patterns of peaks in somatic cell count (SCC) which were based on deviations from the typical lactation curve for SCC. The dataset contained test-day records on SCC in 94 781 lactations of 25 416 cows of different parities. Out of these 94 781 lactations, 41 828 lactations had recordings on occurrence of pathogen-specific CM and on SCC, and 52 953 lactations had recordings on SCC only. A total of 5 324 lactations with cases of CM were recorded. Analysed pathogens were* Staphylococcus aureus, *coagulase negative staphylococci,* Escherichia coli, Streptococcus dysgalactiae, Streptococcus uberis, *and culture-negative samples. Pattern definitions were based on three or five consecutive test-day recordings of SCC. They differentiated between short or longer periods of increased SCC, and also between lactations with and without recovery. Occurrence of pathogen-specific CM and presence of patterns of peaks in SCC were both scored as binary traits. Variance components for sire, maternal grandsire, and permanent animal effects were estimated using AS-REML. The estimated heritability for overall CM was 0·04, and similar heritabilities for pathogen-specific CM were estimated. Heritabilities for the patterns of peaks in SCC ranged from 0·01 to 0·06. Heritabilities for LACSCS were 0·07 to 0·08. Genetic correlations with patterns of peaks in SCC differed for each pathogen. Generally, genetic correlations between pathogen-specific CM and patterns of peaks in SCC were stronger than the correlations with LACSCS. This suggests that genetic selection purely on diminishing presence of peaks in SCC would decrease the incidence of pathogen-specific CM more effectively than selecting purely on lower LACSCS.*

**Keywords:** *genetic correlation, mastitis, pathogens, somatic cell count.*

## Introduction

Current selection indices realize an increase in milk yield and simultaneously monitor udder health by selecting for lower lactational average somatic cell score (LACSCS). Selection for lower LACSCS is expected to be effective in reducing the incidence of clinical *Escherichia coli* mastitis, but less effective in reducing incidences of clinical *Staphylococcus aureus* and *Streptococcus dysgalactiae* mastitis (Nash *et al.*, 2000; de Haas *et al.*, 2002b). Instead of using LACSCS, somatic cell count (SCC) from individual test-day records could be used (Reents *et al.*, 1995). Analysing herd-test-days allows distinguishing between, for example, cows with just one high peak in SCC, and cows with chronically high SCC, although these cows might have the same LACSCS. It could also be hypothesized that patterns of peaks in SCC, which are based on deviations from the typical lactation curve, are more effective selection criteria against (some forms of) clinical mastitis (CM) than LACSCS (Sheldrake *et al.*, 1983; Schepers *et al.*, 1997; de Haas *et al.*, 2002a). Firstly, because different pathological backgrounds of CM result in distinguishable SCC patterns, which cannot be taken into account by LACSCS (Sears *et al.*, 1990; Daley *et al.*, 1991; Vaarst and Enevoldsen, 1997). Secondly, our

phenotypic study of patterns of peaks in SCC and pathogen-specific CM did show that the presence of patterns of peaks in SCC in a lactation was informative for the occurrence of pathogen-specific CM (de Haas *et al.,* 2003). For instance, clinical *E. coli* mastitis was associated with the presence of a short peak in SCC, whereas *S. aureus* was associated with long increased SCC. The objective of this study was to estimate genetic parameters for pathogen-specific CM, LACSCS, and patterns of peaks in SCC. This was done to establish if these SCC patterns provide additional information for selection that aims to decrease genetic susceptibility to (pathogen-specific) CM, in comparison to the information provided by LACSCS alone.

## Material and methods

*Herds*

Records on CM were available from December 1992 till June 1994 on 274 Dutch farms (Barkema *et al.,* 1998). The actual start and end date of the study varied slightly among farms, but all farms participated in the study for 18 months. Lactating cows were housed in free-stall barns and milking parlours were double herringbone or two-sided open tandem. Herds participated in a milk recording system, and annual milk production quotas were between 300 000 and 900 000 kg. The national milk recording system (Royal Dutch Cattle Syndicate (NRS), Arnhem, The Netherlands) provided information on 3- or 4-weekly test-day recordings from 1990 till 1999, from all cows that participated in the longitudinal prospective cohort study of Barkema *et al.* (1998). A record included national cow identification, breed, date of milk recording, date of calving, date of drying off, test-day milk yields (kg milk, fat and protein) and SCC (cells per ml). The breed of the cow was divided into three subclasses. The main breeds were Holstein-Friesian, Dutch-Friesian and Meuse-Rhine-Yssel.

*Bacteriological sampling*

Selection of herds and aseptic sampling procedures have been described previously (Barkema *et al.,* 1998). Data collection of milk samples of quarters with CM depended heavily on the willingness of farmers. Therefore, farmers were continuously encouraged, as described by Barkema *et al.* (1998). During the study period, farmers took milk samples from only those quarters that, in their opinion, had clinical signs of mastitis. Samples were stored in a freezer at the farm (at approx. -20ºC) and were collected for bacteriological examination at intervals of 6 to 8 weeks. Bacteriological culturing of milk samples was performed according to the standards of the National Mastitis Council (Harmon *et al.,* 1990). Briefly, 0·01 ml was cultured and for each culture the number of colony-forming units of each of the bacterial species was counted. Collected data contained information on national cow identification number, date of CM occurrence, quarter location, and result of bacteriological culturing. Pathogen-specific CM was coded as a categorical trait (1 = presence, 0 = absence), irrespective of whether the cow had one or more than one case of CM during the lactation. Therefore, more than one pathogen could be present in a lactation. When separate cases of CM associated with different pathogens occurred in a lactation, or when one case with a mixed culture was isolated, the lactation was scored as 1 for several pathogens. More than one case of CM occurred in 20% of all lactations with CM.

Six groups of pathogens were defined based on their incidence in the data : *Staphylococcus aureus*, coagulase negative staphylococci (CNS), *Escherichia coli*, *Streptococcus dysgalactiae*, and *Streptococcus uberis.* In 19·2% of all bacteriological examinations no pathogen could be isolated (culture-negative), which made the sixth group. A group of remaining records was put together, consisting of lactations with cases of CM caused by other pathogens. In total, 5324 lactations were recorded with cases of CM occurring before 450 days in milk (DIM). This boundary was established using a histogram, and sufficient data was available per DIM until 450 days.

*Data selection*

Originally, phenotypic records on CM and bacteriological characterization were available on 49 529 lactations that had been monitored for at least one day during the study. The data was cleaned up by deleting records of cows with unknown pedigree or with extreme ages at calving (de Haas *et al.,* 2002b). This reduced the dataset to 47 563 lactations from 28 695 cows of different parities. SCC was recorded between January 1990 and December 1999 in 109 335 lactations of these 28 695 cows. Final editing was done by excluding daughters of sires with less than three recordings on CM and less than five recordings on SCC. This reduced the dataset to 94 781 lactations from 25 416 cows of different parities. Out of these 94 781 lactations, 41 828 lactations had recordings on both pathogen-specific CM and SCC, and 52 953 lactations had recordings on only SCC.

Because of the fixed sampling period of health data, variable lengths of DIM, number of days at risk during the study (days on trial; DOT) and number of days in milk at start of the study (days at start; DAS) were present per lactation. Two variables were constructed to be able to adjust for DOT and DAS (De Haas *et al.,* 2002b).

A pedigree file was constructed based on sires and maternal grandsires of cows in the data. The file contained 3285 AI bulls with 2073 sires plus 1934 maternal grandsires (of which 1068 were sires as well), and 346 fathers of the sires or maternal grandsires. The identification of the bull's mother was only included when she had two or more sons in the pedigree file, otherwise she was included as a base parent.

*Definition of SCC patterns*

Patterns of peaks in SCC distinguish between lactations with short or longer periods of increased SCC, and also between lactations with and without recovery within three or five test-day records. Upper and lower thresholds for SCC were set based on literature. Healthy and recovered cows were assumed to have less than 200 000 somatic cells per ml (Dohoo and Leslie, 1991). Infected cows were assumed to produce more than 500 000 cells/ml (Lam *et al.*, 1997). Four patterns of peaks in SCC are described by de Haas *et al.* (2003). The first SCC pattern is referred to as a 'quick recovery pattern' (P1), and describes a quick rise in SCC followed by an immediate decrease in SCC; i.e. consecutive test-day recordings of SCC had to be low-high-low. The second pattern is referred to as a 'slow recovery pattern' (P2) and described a slower increase and decrease in SCC, but still with recovery; i.e. test-day recordings of SCC had to be low, higher, high, lower, and low again. The third pattern (P3) had no restrictions on SCC on the second and fourth test-day record, but the first one had to be low, the third one had to be high, and the fifth one had to be low again. The fourth pattern is referred to as the 'no recovery pattern' (P4) and captured a longer increased SCC; i.e. one test-day with a low SCC recorded followed by four test-days with high SCC, so no recovery took place within four test-day recordings. Patterns of peaks in SCC could appear at each test-day up to 450 DIM. Each pattern of peaks in SCC was scored individually as a categorical trait, so when a SCC pattern was discovered in three or five consecutive test-day records, it was registered as 1, otherwise it was scored as 0.

In the current study, a fifth trait (P5) was defined which indicated whether any of the patterns of peaks in SCC was shown in the lactation or not, without specifying the pattern. Since more than one pattern of peak in SCC could be present in a lactation, the sum of lactations with any of the SCC patterns present is less than the sum of lactations with presence of the individual SCC patterns.

The patterns were compared with the traditionally used LACSCS, based on the first 150 or 305 DIM. An average until 150 DIM was calculated if a cow had three or more recordings of SCC, otherwise a missing value was assigned. Similarly, missing values were replaced with averages until 305 DIM when SCC was measured at least six times. Both lactational averages were log transformed to somatic cell score ($SCS = \log_2(SCC/100\,000) + 3$), from now on referred to as SCS150 and SCS305.

*Statistical analyses*

AS-REML (Gilmour *et al.*, 2002) was used to estimate variance components. Heritabilities were estimated in univariate analyses, using a linear model ($Y$) for SCS150 and SCS305, and using a logistic model (Logit($Y$)) for P1, P2, P3, P4, P5 and pathogen-specific CM. Cows with missing values for SCS150, SCS305, SCC patterns or pathogen-specific CM were still included in the analyses. The model included random effects for sire and maternal grandsire (MGS) and an effect for animal, to account for the permanent animal effects across repeated lactations. The model used was:

$$Y \text{ or } \text{Logit}(Y) = \mu + \text{fixed effects} + S_{sire} + \tfrac{1}{2}S_{mgs} + \text{PERM}_{animal} + e$$

The random sire effect was identified by the subscripts for sire and MGS; $S_{sire}$ and $S_{mgs}$, respectively. The sire effects were linked using the relationship matrix, and were assumed to be normally distributed with $\text{var}(S_{sire\ or\ mgs}) = \sigma^2_s$. Permanent animal effects contain environmental effects common to different lactations and genetic effects not covered by sire and MGS, like a dam-component, dominance, and Mendelian sampling terms. This was assumed to be normally distributed as well, with $\text{var}(\text{PERM}_{animal}) = \sigma^2_{Ea}$. For the logistic model, the residual variance ($\sigma^2_\varepsilon$) was fixed on 3·29; N(0, 3·29) (Gilmour *et al.*, 2002). Residual covariances can only be estimated for those lactations with information on both pathogen-specific CM and SCC traits (i.e. P1, P2, P3, P4, P5, SCS150 or SCS305).

Fixed effects included were herd (with 274 levels), an interaction between year and season of calving (YS, with 43 classes), parity (with four classes, where the last class contains all parities ≥ 4), and the fraction of Holstein-Friesian genes (with nine classes, for 0, 1/8, …, 8/8). For CM, polynomials of order 1, 2 and 4 were included for age at calving, DAS and DOT, respectively. For SCS150, SCS305, and SCC patterns, a polynomial of order 4 for age at calving was included. Order of the polynomials was established by stepwise inclusion of higher order regression coefficients (forward and backward elimination) till the estimated regression coefficient did not differ significantly from zero any more.

**Table 1** *Number of lactations with presence of patterns of peaks in somatic cell count (SCC)† and with occurrence of pathogen-specific clinical mastitis, standard deviations for additive genetic ($\sigma_a$) and permanent animal ($\sigma_{Ea}$) effects, and heritability ($h^2$), all from univariate analyses, with standard errors in parentheses*

| | No. | $\sigma_a$ | $\sigma_{Ea}$ | $h^2$ |
|---|---|---|---|---|
| Pattern 1 | 7540 | 0·17 | 0·32 | 0·01 (0·01) |
| Pattern 2 | 1080 | 0·36 | 0·63 | 0·03 (0·02) |
| Pattern 3 | 5951 | 0·16 | 0·34 | 0·01 (0·01) |
| Pattern 4 | 3441 | 0·50 | 0·87 | 0·06 (0·02) |
| Any pattern | 12 535 | 0·14 | 0·45 | 0·02 (0·01) |
| Clinical mastitis | 5324 | 0·39 | 0·51 | 0·04 (0·01) |
| *Staphylococcus aureus* | 1419 | 0·42 | 0·54 | 0·05 (0·02) |
| Coagulase negative staphylococci | 453 | 0·59 | 0·37 | 0·10 (0·06) |
| *Escherichia coli* | 1335 | 0·44 | 0·50 | 0·05 (0·02) |
| *Streptococcus dysgalactiae* | 844 | 0·45 | 0·43 | 0·06 (0·03) |
| *Streptococcus uberis* | 464 | 0·41 | 0·55 | 0·05 (0·04) |
| Other streptococci | 637 | 0·25 | 0·47 | 0·02 (0·03) |
| Culture-negative samples | 1026 | 0·43 | 0·40 | 0·05 (0·03) |
| Other pathogens | 675 | 0·44 | 0·19 | 0·06 (0·04) |

† Pattern 1: quick recovery pattern (low-high-low SCC); pattern 2: slow recovery pattern (low-higher-high-lower-low SCC); pattern 3: (low-no restrictions-high-no restrictions-low SCC); pattern 4: no recovery pattern (low-high-high-high-high SCC)); any pattern: presence of any of the earlier described patterns. Since more than one pattern of peak in SCC could be present in a lactation, the sum of lactations with any of the SCC patterns present is less than the sum of lactations with presence of the individual SCC patterns.

Bivariate analyses were carried out to estimate correlations between SCC patterns and pathogen-specific CM, using a linear model for all traits. Combined linear and logistic models were also used, in which either the pathogens or the SCC patterns were treated as binary trait, and the other trait was assumed to be normally distributed. The estimated genetic correlations were similar to those originating from the complete linear model, and therefore only the estimated parameters from the complete linear model are shown. Fixed effects were the same as mentioned for the univariate analyses.

*Calculation of genetic parameters*

Genetic parameters were calculated from the estimated variance components. Additive genetic variance ($\sigma^2_a$) was calculated by multiplying sire variance by four. The phenotypic variance was the sum of (1) sire variance multiplied by 1·25, where 1·25 was included because MGS was fitted in the model separately, (2) permanent animal variance, and (3) residual variance. Division of additive genetic variance by phenotypic variance resulted in the heritability. Genetic and phenotypic correlations were estimated using the corresponding variances

**Table 2** *Estimated genetic correlations below diagonal, and phenotypic correlations above diagonal from bivariate analyses between somatic cell count (SCC) patterns† and somatic cell score of lactational average cell counts up to 150 or 305 days in milk (SCS150 and SCS305, respectively), with their respective standard errors in parentheses*

| | Pattern 1 | Pattern 2 | Pattern 3 | Pattern 4 | Any pattern | SCS150 | SCS305 |
|---|---|---|---|---|---|---|---|
| Pattern 1 | | 0·01 (0·003) | 0·50 (0·003) | –0·03 (0·003) | 0·75 (0·003) | 0·21 (0·003) | 0·21 (0·003) |
| Pattern 2 | 0·99 ‡ | | 0·48 (0·003) | 0·24 (0·003) | 0·27 (0·003) | 0·10 (0·003) | 0·10 (0·003) |
| Pattern 3 | 0·97 (0·12) | 0·99 ‡ | | 0·09 (0·003) | 0·66 (0·003) | 0·23 (0·003) | 0·22 (0·003) |
| Pattern 4 | 0·31 (0·24) | 0·62 (0·24) | 0·88 (0·17) | | 0·48 (0·003) | 0·31 (0·003) | 0·35 (0·003) |
| Any pattern | 0·83 (0·13) | 0·99 ‡ | 0·99 ‡ | 0·97 (0·04) | | 0·39 (0·003) | 0·41 (0·003) |
| SCS150 | 0·31 (0·23) | 0·99 ‡ | 0·89 (0·13) | 0·84 (0·06) | 0·76 (0·08) | | 0·88 (0·003) |
| SCS305 | 0·02 (0·24) | 0·98 (0·15) | 0·74 (0·20) | 0·84 (0·06) | 0·67 (0·10) | 0·97 (0·01) | |

† Pattern 1: quick recovery pattern (low-high-low SCC); pattern 2: slow recovery pattern (low-higher-high-lower-low SCC); pattern 3: (low-no restrictions-high-no restrictions-low SCC); pattern 4: no recovery pattern (low-high-high-high-high SCC); any pattern: presence of any of the earlier described patterns.
‡ These genetic correlations were fixed at boundary.

and covariances. Standard errors are provided by AS-REML, and give an indication of the accuracy of the estimates. Tests to assess statistical significance are not straightforward, since the distribution of the sampling variation is not normal.

## Results

Heritabilities for patterns of peaks in SCC ranged from 0·01 to 0·06 (Table 1). Heritabilities were 0·07 (s.e. 0·01) for SCS150 and 0·08 (s.e. 0·01) for SCS305. Phenotypic correlations between two individual SCC patterns ranged from –0·03 to 0·50 (Table 2). Genetic correlations were high (0·74 to 0·99) between SCS150 or SCS305 and P2, P3, or P4 (Table 2), but low between P1 and SCS150 or SCS305 (i.e. 0·31 and 0·02, respectively). Genetic correlations were high between P1-P2, P1-P3 and P3-P4 (0·99, 0·97 and 0·88, respectively), whereas genetic correlations between P1-P4 and P2-P4 were moderate (0·31 and 0·62, respectively) (Table 2).

Phenotypic correlations between overall CM and LACSCS were positive; i.e. 0·26 for both SCS150 and SCS305, and ranged from 0·04 to 0·12 between overall CM and patterns of peaks in SCC (Table 3). Positive phenotypic correlations between pathogen-specific CM and SCS150 or SCS305 ranged from 0·06 to 0·20, indicating that LACSCS was higher in lactations with CM than in lactations without CM. Between pathogen-specific CM and SCC patterns the phenotypic correlations ranged from 0·01 to 0·10. These positive correlations indicated that on average the proportion of lactations with presence of patterns of peaks in SCC was higher when considering all lactations with occurrence of pathogen-specific CM (no. = 5324) than when considering all lactations without occurrence of pathogen-specific CM

**Table 3** *Estimated phenotypic correlations from bivariate analyses between pathogen-specific clinical mastitis, recorded in the first 450 days in lactation, lactational average somatic cell scores, averaged over test-day records up to 150 and 305 days in lactation (SCS150 and SCS305, respectively), and somatic cell count (SCC) patterns*†

| | Pattern 1 | Pattern 2 | Pattern 3 | Pattern 4 | Any pattern | SCS150 | SCS305 |
|---|---|---|---|---|---|---|---|
| Clinical mastitis | 0·11 | 0·04 | 0·12 | 0·11 | 0·18 | 0·26 | 0·26 |
| *Staphylococcus aureus* | 0·03 | 0·03 | 0·05 | 0·10 | 0·10 | 0·18 | 0·20 |
| Coagulase negative staphylococci | 0·03 | 0·02‡ | 0·02 | 0·05 | 0·05 | 0·09 | 0·08 |
| *Escherichia coli* | 0·08 | 0·02 | 0·07 | 0·02 | 0·10 | 0·10 | 0·09 |
| *Streptococcus dysgalactiae* | 0·03 | 0·02 | 0·05 | 0·05 | 0·07 | 0·12 | 0·11 |
| *Streptococcus uberis* | 0·04 | 0·01 | 0·04 | 0·05 | 0·07 | 0·08 | 0·09 |
| Culture-negative samples | 0·04 | 0·01 | 0·04 | 0·02 | 0·05 | 0·07 | 0·06 |
| Other pathogens | 0·03 | 0·01 | 0·04 | 0·03 | 0·06 | 0·08 | 0·08 |

† Pattern 1: quick recovery pattern (low-high-low SCC); pattern 2: slow recovery pattern (low-higher-high-lower-low SCC); pattern 3: (low-no restrictions-high-no restrictions-low SCC); pattern 4: no recovery pattern (low-high-high-high-high SCC); any pattern: presence of any of the earlier described patterns.
‡ s.e.= 0·00; for all other correlations s.e.= 0·01.

**Table 4** *Estimated genetic correlations from bivariate analyses between pathogen-specific clinical mastitis, recorded in the first 450 days in lactation, lactational average somatic cell scores, averaged over test-day records up to 150 and 305 days in lactation (SCS150 and SCS305, respectively), and somatic cell count (SCC) patterns*†*, with their respective standard errors in parentheses*

| | Pattern 1 | Pattern 2 | Pattern 3 | Pattern 4 | Any pattern | SCS150 | SCS305 |
|---|---|---|---|---|---|---|---|
| Clinical mastitis | 0·85 (0·18) | 0·99 ‡ | 0·99 ‡ | 0·76 (0·13) | 0·90 (0·08) | 0·74 (0·09) | 0·50 (0·13) |
| *Staphylococcus aureus* | 0·66 (0·27) | 0·98 (0·27) | 0·93 (0·19) | 0·50 (0·22) | 0·62 (0·20) | 0·53 (0·18) | 0·26 (0·19) |
| Coagulase negative staphylococci | 0·99 ‡ | 0·99 ‡ | 0·97 (0·18) | 0·44 (0·30) | 0·89 (0·20) | 0·99 ‡ | 0·26 (0·25) |
| *Escherichia coli* | 0·92 (0·25) | 0·99 (0·29) | 0·85 (0·22) | 0·86 (0·14) | 0·90 (0·13) | 0·68 (0·17) | 0·54 (0·20) |
| *Streptococcus dysgalactiae* | 0·27 (0·38) | 0·65 (0·37) | 0·70 (0·31) | 0·40 (0·27) | 0·50 (0·25) | 0·28 (0·22) | 0·18 (0·23) |
| *Streptococcus uberis* | 0·49 (0·58) | 0·82 (0·60) | 0·99 ‡ | 0·68 (0·41) | 0·72 (0·42) | 0·73 (0·37) | 0·59 (0·40) |
| Culture-negative samples | 0·50 (0·31) | 0·59 (0·42) | 0·56 (0·34) | –0·05 (0·25) | 0·31 (0·26) | 0·38 (0·20) | 0·29 (0·21) |
| Other pathogens | 0·55 (0·35) | 0·47 (0·38) | 0·55 (0·37) | 0·44 (0·24) | 0·48 (0·25) | 0·51 (0·19) | 0·45 (0·20) |

† Pattern 1: quick recovery pattern (low-high-low SCC); pattern 2: slow recovery pattern (low-higher-high-lower-low SCC); pattern 3: (low-no restrictions-high-no restrictions-low SCC); pattern 4: no recovery pattern (low-high-high-high-high SCC); any pattern: presence of any of the earlier described patterns.
‡ These genetic correlations were fixed at boundary.

(no. = 36 504) (18 *v.* 8%, 3 *v.* 1%, 17 *v.* 6%, and 10 *v.* 3% for P1, P2, P3 and P4, respectively).

Genetic correlations between overall CM and patterns of peaks in SCC were stronger than the genetic correlations between CM and SCS150 or SCS305 (Table 4). In general, this holds for pathogen-specific CM as well, especially for cases of CM associated with *S. aureus*, CNS, *E. coli* and *Str. dysgalactiae*. *Streptococcus uberis* and culture-negative CM showed similar genetic correlations with both patterns of peaks in SCC and SCS150 or SCS305. Genetic correlations of pathogen-specific CM with SCS150 were always stronger than correlations with SCS305 (Table 4).

## Discussion

The objective of the study was to estimate genetic parameters for pathogen-specific CM, LACSCS, and patterns of peaks in SCC. This objective can be split up in three questions : i.e. (1) do these SCC patterns differ genetically from LACSCS, (2) is genetic selection on SCC patterns more effective to decrease the incidence of overall CM, than selection on LACSCS, (3) do these SCC patterns provide additional information for selection that aims to decrease susceptibility of pathogen-specific CM, in comparison with the information provided by LACSCS alone?

*SCC patterns* v. *lactational average SCS*

Robertson and Lerner (1949) showed that parameter estimates from categorical traits using a linear model are frequency dependent, and should be transformed from the observable to the underlying scale for comparison purposes. Therefore, in this study a generalized linear model has been applied to the underlying liability scale, to estimate the (co)variance matrices for the categorically scored SCC patterns. Heritabilities for the patterns of peaks in SCC seem to be only slightly lower than those estimated for normally distributed LACSCS. However, if the estimates of heritabilities for the patterns of peaks in SCC had originated from analyses with a linear model, they would have been much lower than the estimates for LACSCS. Estimated heritabilities for SCS150 and SCS305 are low at approximately 0·08, but consistent with literature estimates. In a review of literature, Mrode and Swanson (1996) found a weighted $h^2$ estimate of 0·11 (s.e. 0·04).

Phenotypic correlations between two patterns of peaks in SCC were low. The strongest phenotypic correlations were estimated between P1 and P3 and between P2 and P3. The overlap between the definitions of P1 and P3 and of P2 and P3 was the main explanation for this higher phenotypic correlation. No restrictions were put on the second and fourth consecutive test-day for P3. When low SCC were recorded on these test-days, this overlapped with the definition for P1, when SCC between the lower and upper thresholds were recorded, this overlapped with the definition of P2. It is unlikely that both P1 and P2, or P1 and P4, or P3 and P4 are present in the same lactation, because it requires many test-day records to have both patterns present one after another. Phenotypic correlations between these SCC patterns were therefore low. The 'slow recovery pattern' is less phenotypically correlated with both SCS150 and SCS305 than the 'quick recovery pattern'. This was not expected based on comparison of the calculated mean SCS150 and SCS305 in lactations with presence of P1 (3·98 and 4·26, respectively), and in lactations with presence of P2 (4·53 and 4·69, respectively). A possible explanation for the low phenotypic correlation might be the low incidence of P2, since in most lactations P2 = 0, and in only a few P2 = 1. Therefore, relatively, only a few values of SCS150 or SCS305 are associated with P2 = 1, and many values are associated with P2 = 0.

Genetic correlations between P1, P2 and P3 were high, implying these traits were similar to each other, which might be due to the existing overlap between the definitions of these patterns of peaks in SCC. The low genetic correlations between the 'quick recovery pattern' and SCS150 or SCS305 imply that these are different traits. This can phenotypically be explained by a possible smaller effect of one single increase in SCC, compared to the effect of longer periods of increased SCC. As a result of this, selection for lower LACSCS will probably not accomplish the same effect as selection on less presence of 'quick recovery patterns' in the lactation. Ideally, a cow should recover quickly from an infection once she gets infected. It can be hypothesized that the 'quick recovery pattern' belongs to cattle that recover quickly from an infection. Therefore, genetic selection for a lower presence of 'quick recovery patterns' might reduce the cow's abilities for a quick clearance of the infection.

*Use of SCC patterns to decrease incidence of CM*

The estimated genetic correlations fitted very well in the range of estimated genetic correlations between CM and SCC in other studies (0·3 to 0·9), which is reviewed by Mrode and Swanson (1996) and Emanuelson (1997). Correlations of 0·74 and 0·50 were estimated between CM and SCS in the first 150 and 305 DIM, respectively. This suggests that selection for lower SCS, especially during early lactation, also decreases the incidence of CM. Similar trends were reported by Emanuelson *et al.* (1988).

Incidence of CM is higher in early lactation, as we have shown for this data (de Haas *et al.,* 2002a), which might explain the higher correlation between CM and SCS150, compared with the correlation between CM and SCS305. In comparison with SCS150, the presence of any pattern of peaks in SCC was more strongly correlated with occurrence of CM. It seems that selection against any kind of deviation from the typical lactation curve for SCC would therefore be more effective in decreasing the incidence of CM, than selection for lower LACSCS.

*Use of SCC patterns to decrease incidence of pathogen-specific CM*

Genetic correlations between pathogen-specific CM and patterns of peaks in SCC differed among pathogens, but were not as clear-cut as the phenotypic associations that were reported in an earlier study (de Haas *et al.,* 2003). Genetic correlations between pathogen-specific CM and patterns of peaks in SCC were generally stronger than the correlations with SCS150 or SCS305, as was also observed for overall CM. This suggests that genetic selection purely on diminishing presence of peaks in SCC would decrease the incidence of cases of CM caused by all pathogens more effectively than selecting purely on lower LACSCS, but standard errors are large, so caution should be taken here.

The definitions of the currently analysed patterns of peaks in SCC were based on biological understanding of pathogens and the immune system of the cow. Apparently, these peaks do not distinguish clearly between resistance to certain pathogens on a genetic level. For example, from a biological point of view intramammary infections (IMI) with *S. aureus* can be characterized by a long duration and high SCC (Sears *et al.,* 1990; Daley *et al.,* 1991), which we confirmed at phenotypic level in a previous study (de Haas *et al.,* 2003). In general, the estimated phenotypic correlations in this study were not high, but the highest for *S. aureus* was found with the 'no recovery pattern'. Unfortunately this trend was not confirmed by the genetic correlations. Instead, *S. aureus* CM shows the weakest genetic correlation with the 'no recovery pattern' (P4), and not the strongest. On the other hand, *E. coli* CM are typically acute cases (Vaarst and Enevoldsen, 1997), which was also confirmed in the phenotypic study (de Haas *et al.,* 2003). On the genetic level a strong correlation between *E. coli* CM and the 'quick recovery pattern' (P1) was estimated. The higher correlation between P1 and *E. coli* CM is likely to come from a generally stronger association between *E. coli* CM and all SCC patterns, rather than specific properties of P1. So, maybe newly defined traits for SCC to be used as indirect traits in genetic selection programs should not only be based on biological backgrounds. Suggestions for other traits have been given in other studies (Heuven, 1987; Detilleux *et al.,* 1997; Schepers *et al.,* 1997).

Detilleux *et al.* (1997) concluded that analyses of SCC as candidate for selection against mastitis resistance could be improved by choosing better measures of SCC. These measures should contain all non-genetic factors that cause variation in SCC and methods of genetic epidemiology could be used as well. Depending upon the goal of the study, various ways of using SCC may be proposed for udder health surveillance. Examples they proposed were (1) proportion of test-day SCC above or below a certain limit, (2) direction and rate of change in test-day SCC, (3) time until SCC reach a given limit, (4) difference between observed SCC and SCC expected under healthy conditions, (5) area under (parts of) the lactation curve of SCC, (6) rolling averages, and (7) DIM that the increase in SCC happens. In relation to this, information on DIM at occurrence of CM could be taken into account as well, since recording increased SCC on test-days depend on a) the day of occurrence of CM in relation to test-day recordings and b) the duration of increased SCC as a result of pathogen-specific CM. The 'given limit' in the third suggestion of Detilleux *et al.* (1997) might, for instance, be the maximal recorded SCC during a lactation, which might be informative as to the mastitis-causing pathogen. On the one hand it was hypothesized that the higher peaks were associated with clinical *E. coli* mastitis, as these cases are known to be acute. However, in our study on the effects of pathogen-specific CM on the lactation curve for SCC we found that clinical *E. coli* mastitis did not have the strongest effect on SCC (de Haas *et al.,* 2002a). Instead, cases of CM associated with either *Str. dysgalactiae* or *Str. uberis* resulted in the highest peaks in SCC. The method we have presented in the current study is a combination of the second and fourth suggestion of Detilleux *et al.* (1997). Including information on DIM at increase in SCC and DIM at occurrence of CM might improve the results.

Schepers *et al.* (1997) also provided alternative measures of SCC, based on the evaluation of the thresholds for IMI based on SCC. Twelve alternative SCC test statistics were calculated, divided into three groups : (1) three thresholds, for which identification of IMI was based on different fixed SCC values, (2) five thresholds, that were specific to parity, for which identification of IMI was based on the lactation curve of SCC, (3) four thresholds for which identification of new IMI was based on deviation between current and previous samples in the same lactation. The use of SCC thresholds for specific parities and stages of

lactation to detect IMI improved the quality of parameters only slightly over a fixed threshold of 200 000 cells per ml (Dohoo and Leslie, 1991). The third option of Schepers *et al.* (1997) is similar to the method used in the current study.

Finally, Heuven (1987) analysed test-day records of SCC to predict the presence of pathogens, and developed a method to identify abnormal observations of SCC, in order to exclude them from the data set. An observation was considered to be abnormal on the basis of its deviation from the typical lactation curve. While using this exclusion method, he concluded that cows with either a high average SCC or a test-day with a high deviation from the typical lactation curve for SCC were more likely to be treated for CM. A single test-day with a high SCC recorded may not affect the lactation average SCC much, whereas longer increased SCC will affect the lactation average SCC eventually. Therefore, by selecting for lower (arithmetic) mean SCC during lactation the group of cows with a single high deviation from the typical lactation curve for SCC might be missed. However, these cows might still be more genetically susceptible to CM, as they might become infected more often, making it more likely that they would have elevated SCC on a test-day. In the current study the deviation from the typical lactation curve for SCC is taken into account, and therefore, the group of cows with one single high SCC recorded on a test-day can be identified.

In summary, selection for lower SCS, especially during early lactation, will decrease the incidence of CM, but in comparison with SCS150, the presence of any of the patterns of peaks in SCC is more strongly correlated with occurrence of CM. Genetic correlations between pathogen-specific CM and patterns of peaks in SCC should be interpreted with caution, because of high standard errors. However, the current results indicate a stronger genetic correlation between overall CM and presence of any pattern of peaks in SCC, and therefore encourage further research in patterns of peaks in SCC for genetic selection or mastitis control programmes. Further optimization includes increasing the accuracy of the estimated (co)variance matrices by enlarging the dataset for SCC. Other definitions of new traits for SCC (i.e. not based on biological backgrounds) as indirect traits in genetic selection programmes should be considered as well.

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