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Genetic and Phenotypic Relationships Among Endocrine and Traditional Fertility Traits and Production Traits in Holstein-Friesian Dairy Cows

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ABSTRACT

The objective of this study was to estimate the heritability of a number of traditional and endocrine fertility traits in addition to d-56 predicted milk yield (MY56), and the genetic and phenotypic correlations between these traits. Various fixed effects such as season, year, herd, lactation number, diet, percentage Holstein (PCH) of the cow, and occurrence of uterine infection (UI), dystocia (DYS), and retained placenta (RP) were also investigated. Data collected for 1212 lactations of 1080 postpartum (PP) Holstein-Friesian dairy cows in eight commercial farms between 1996 and 1999 included thrice weekly milk progesterone samples, calving and insemination dates, various reproductive health records, monthly/bimonthly production records, three-generation pedigrees, and PCH information. Genetic models were fitted to the data to obtain heritabilitites and correlations using ASREML. Estimates of heritability for interval to commencement of luteal activity PP (lnCLA), length of the first luteal phase PP (lnLutI) and occurrence of persistent CL type I (PCLI) were 0.16, 0.17, and 0.13, respectively. Heritabilities for pregnancy to first service (PFS), interval to first service (IFS), and MY56 were 0.14, 0.13, and 0.50, respectively. Genetic regressions of lnCLA and lnLut1 on PTA of the sire for milk, fat, and protein yields, and PIN95 were investigated. Regressions of lnCLA were positive and significant on fat yield, while regressions of lnLut1 on both protein yield and PIN95 were negative and significant. Genetic correlations of endocrine fertility traits (lnCLA, lnLutI, and PCLI) with MY56 were high (0.36, $P < 0.05$; –0.51, $P < 0.05$; and –0.31, $P < 0.1$, respectively). Percentage Holstein of the cows had no significant effect on any of the fertility parameters monitored. This work emphasizes the strong genetic correlation of fertility with production traits and, therefore, highlights the urgent requirement for selective breeding for fertility in the United Kingdom. The high heritability of endocrine fertility traits stress their potential value for inclusion in a selection index to improve fertility.

(**Key words:** fertility, progesterone, genetic correlation, milk production)

INTRODUCTION

Infertility in dairy cattle represents a problem of increasing importance, and causes considerable losses in the dairy industry. From 1975 to 1997, pregnancy rates fell phenotypically (by 0.45% per annum) in the United States (Butler and Smith, 1989; Beam and Butler, 1999). Similarly, over the last 20 yr, the calving rate to first service in the United Kingdom has declined at a derived average of 1.0% per annum, and the typical herd now has a first service calving rate of approximately 40% (Darwash et al., 1999; Royal et al., 2000a; Ball, personal communication). This decline has coincided with the gradual replacement of the British Friesian by the Holstein, and the continuing drive by breeding companies to increase genetic merit for milk production. However, although many Scandinavian countries, France, Germany, Israel, and The Netherlands have developed genetic evaluations for sires based on their daughters' fertility (See Linde and Philipsson, 2001; Pryce et al., 2000), no one has attempted to incorporate fertility into UK breeding programs.

One barrier to the inclusion of fertility in breeding programs in the United Kingdom has been the poor quality of insemination records. For example, UK national data consist of all insemination data, some insemination data, or only the insemination data leading

to a subsequent pregnancy (Pryce et al., 2000). Consequently, analysis of this type of data can lead to unreliable or biased results. Measurement of fertility with milk progesterone data may offer an alternative to, or may complement, high quality records on insemination. An analysis of milk progesterone concentrations during 2503 lactations in British Friesian cows (1975 to 1982) showed that the interval to commencement of luteal activity postpartum (**CLA**) was phenotypically associated with traditional measurements of fertility and had moderate heritability (0.21), much higher than the heritability of other traditional fertility measures (typically, $h^2 < 0.05$; Darwash et al., 1997a, 1997b, 1998). This offered the possibility of using milk progesterone measurements as an early aid in culling subfertile cows, or in evaluating sires based on their daughters' endocrine characteristics in a progeny test.

These investigations were extended to the more modern UK Holstein dairy cow between 1995 and 1999 (Royal et al., 2000a, 2000b, 2000c). As well as documenting the sharp phenotypic decline in fertility, a comparison of the data from Holstein-Friesians and British Friesians identified an increase in the proportion of animals with one or more atypical ovarian hormone patterns from 32% to 44% ($P < 0.005$). In particular, the incidence of delayed luteolysis during the first cycle postpartum (**PCLI**, 7.3% to 18.2%; $P < 0.005$) and during subsequent cycles increased (**PCLII**, 6.4% to 16.8%; $P < 0.005$), although the incidence of prolonged anovulation postpartum (delayed ovulation; **DOVI**) and prolonged inter-luteal intervals (delayed ovulation; **DOVII**) did not alter significantly.

While these observations suggest an unfavorable phenotypic association between atypical ovarian hormone patterns and fertility, phenotypic and genetic (co)-variances have not been estimated. This is largely because, until now, a well-structured and well-recorded dataset has not been available to permit such analyses. Genetic (co)variances are the critical measure of how such traits can be combined with others of economic importance to accomplish selection objectives. Therefore, the objectives of this study were to estimate genetic parameters for a number of endocrine and traditional measures of fertility in addition to predicted peak milk yield and to investigate the genetic relationships among them.

MATERIALS AND METHODS

Database Formation

Pedigree and performance records. Data on lactation and reproductive performance from two 'research' databases (University of Nottingham and Roslin Institute) and additional information from two 'commercial'
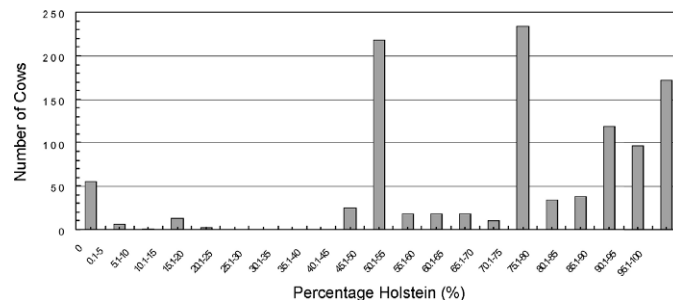

Figure 1. The distribution of Holstein genes in the cows monitored.

databases [National Milk Records (NMR, Chippenham, United Kingdom) and Holstein, United Kingdom and Ireland (HUKI, Rickmansworth, United Kingdom)] were combined into a single database using Microsoft Access. The information from the Nottingham and Roslin databases related to 811 and 408 lactations, respectively, collected between October 1996 and March 1999.

The HUKI database provided three-generation pedigrees for all cows in the study (i.e., up to and including great-grandparents) where herd book numbers were available. For all other cows, two-generation pedigrees were obtained for their sires from the HUKI database, together with any known dam pedigree up to the limit of the great-grandparents of the study cow. The NMR database provided milk records after permission had been received from herd owners for all cows except those from Roslin Institute.

The Holstein percentages (**PCH**) of all cows in the study were either obtained directly from the HUKI database or calculated directly from the known pedigree. The distribution of PCH (for the cows monitored) in the database is shown in Figure 1. Approximately 85% of the sires used in the current database were 100% Holstein and 7% were 100% Friesian.

PTA were obtained for the sires used from the Animal Data Centre (ADC, Chippenham, United Kingdom). Those available were milk, fat, and protein yield and a profit index (**PIN95**), which is based on yield traits and reflects the UK economic value (minimum, maximum, and standard deviations for milk, fat and protein yield, and PIN95 were: –628, 1209, and ± 386.14 kg; –27, 36, and ± 12.21 kg; –20, 36, and ± 11.32 kg; and –£76, –129, and ± 41.13, respectively). Sixteen sires (73 cows) had no available PTA data.

Progesterone, veterinary, and insemination information. Progesterone profiles were available on all cows in the database as a result of progesterone measurement in milk samples taken thrice weekly as described by Royal et al. (2000a). Veterinary treatments for reproductive disorders have been sourced and inter-
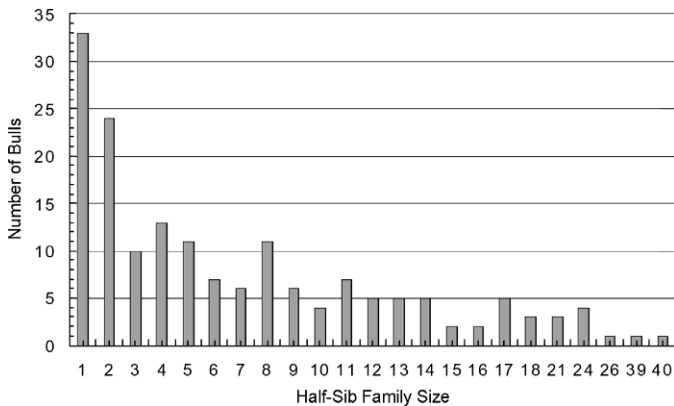
Figure 2. The distribution of half-sib family sizes (n = 169) in the database.

preted for both 'research' databases, and these details included in the combined database.

Endocrine fertility parameters investigated from the combined database include CLA (days; n = 1212), length of the first luteal phase (**LUTI**, days; n = 1146), and the occurrence of PCLI (scored as zero for absence and one for presence; n = 1146), which is a consequence of an extended LUTI. The precise definitions of these parameters are given in Royal et al. (2000a).

Traditional fertility parameters investigated were interval to first service (**IFS**, days; n = 1121) and pregnancy rate to first service (**PFS**, scored as zero or one; n = 667). Approximately 5% of inseminations were at an inappropriate stage of the estrous cycle judged from the progesterone profiles (i.e., where there was no chance of a pregnancy being established). These were eliminated from the estimation of IFS and PFS. The data analyzed for PFS were also limited because only a subset of the data included the necessary information. Pregnancy was confirmed by nonreturn to estrus accompanied by a subsequent parturition, with the exception of 14 cases (palpation/scanning was used). Pregnancy failure was confirmed by a fall in milk progesterone following a service and/or a subsequent service together with accompanying calving dates.

The production parameter representing milk yield was chosen as predicted milk yield on d 56 (**MY56**; kg). Day 56 was chosen because it was close to the time of peak yield for all the herds in the dataset. Estimation of MY56 is described below.

Statistical Analyses

The total number of records used in the analyses was 1212 lactations recorded from 1080 cows in eight herds, forming 169 paternal half-sib groups (group sizes between one and 40). Figure 2 illustrates the distribution

of paternal half-sib family sizes in the database. A total of 923 maternal half-sib groups were present (including singleton groups) with the largest maternal half-sib group size of three. It was not possible to identify two of the 169 sires and 31 of the dams; those unidentified were assumed to be unique. Milk yield information was not available for 60 lactations, reducing the number of lactations available for the MY56 analysis to 1152.

Mixed linear models were fitted to the data using the restricted maximum likelihood method. ASREML software [(A. R. Gilmour, R. Thompson, B. R. Cullis, and S. Welham; 2001), and *ASREML User's Manual* (ftp://ftp.res.bbsrc.ac.uk/pub/aar)] were used to conduct univariate and bivariate analyses of traits in the database in order to estimate both variance components and fixed effects. GENSTAT software (Lawes Agricultural Trust, 1997) was used to implement a model of lactation curves to the test-day records for predicting yields on a given day postpartum for use in subsequent analyses.

Principal fixed and random effects used in analyses. (See the Appendix for a detailed model equation.) The fixed effects analyzed in the models (at least initially) were: herds (7 df), diet within herd [(15 df), lactation number (8 df), year of calving (3 df), season of calving (3 df; December–February, March–May, June–August, September–November)], occurrence of retained placenta (1 df), occurrence of dystocia (1 df), occurrence of uterine infection (1 df), and PCH fitted as a regression (1 df). The possible existence of genetic components of retained placenta, uterine infection and dystocia were investigated before their use as fixed effects (see Results section).

The inclusion of diet in the model ensured that the impact of herds feeding experimental diets or using characteristic management protocols during the trial was minimized (ADAS Bridgets, 10 diets; Nottingham University, three diets; Roslin Institute, three diets). This identifiable source of variation was treated as a fixed, nuisance effect. The inclusion of PCH in the model as a regression provided an additive breed difference between Holstein and Friesian, over and above any genetic variation within the breeds.

The two- and three-way interactions among herds, years, and seasons were fitted throughout as random effects for each trait, at least in initial models. In all models, genetic relationships were modeled by the relationship matrix calculated from the three-generation pedigrees and scaled by σ_A^2, the additive genetic component within breeds. This variance component was assumed to be equal for Holstein and Friesian. Permanent environmental effects were also investigated initially, as repeated measurements for the same cows were contained within the database.

The significance of fixed and random effects were assessed by Wald tests and likelihood-ratio tests, respectively. Both are approximately distributed as chi-squared. Functions of interest were the phenotypic variance $\sigma_P^2 = \sigma_A^2 + \sigma_C^2 + \sigma_E^2$ (where σ_A^2, σ_C^2 and σ_E^2 represent additive genetic, permanent environmental and error variation, respectively), and heritability (σ_A^2/σ_P^2). Standard errors for fixed effects and for functions of the variance components were obtained using AS-REML procedures.

The heritability estimates for CLA and LUTI were sensitive to transformation (observed, natural logarithm, and reciprocal) in the current and previous analyses (Darwash et al., 1997b). These transformations weighted the phenotypic distributions in such a way that the shorter intervals received more weighting as the transformation moved from the observed to the reciprocal scale. The natural logarithm of CLA is used in the present analyses (lnCLA) since Darwash et al. (1997b) concluded that the $\log_e$ transformation fitted the model better than either observed or reciprocal transformations, and comparisons with this previous study are, therefore, more direct. The natural logarithm of LUTI was taken to keep the analysis in line with CLA.

Once the initial analyses had provided basic models for the traits, further analyses were carried out to explore genetic relationships among traits by introducing PTA as covariates into the model and bivariate analyses. The cows used in the genetic evaluations resulting in the PTA for yield formed only a small component of the total information in the evaluation. Therefore, the results assume that significant regressions are indicative of genetic relationships.

Prediction of 56-d yield. In analyses involving milk yield, the trait used for analysis was the predicted 56-d yield (MY56). This was estimated from a model of phenotypic yield based upon Wood's curve (Wood, 1967), with random regressions for cows and lactations within cows (D. Waddington, unpublished). The parameters used for implementing the model were derived from an extensive analysis of the NMR database involving 30,000+ monthly records.

RESULTS

Numbers of records, means, phenotypic standard deviations, heritabilities, and genetic and phenotypic correlations are summarized in Tables 1 and 2 for endocrine and traditional fertility traits in addition to peak milk yield. The main findings are described below.

Analysis of Genetic Variation in Postpartum Reproductive Problems

Before their use as fixed effects in subsequent analyses, the magnitude of genetic variation in reproductive problems recorded postpartum was examined. In all cases, the genetic component was small and not significant, and it was assumed that any genetic influence might be ignored in the current analysis.

Analysis of Genetic Variation in Endocrine Fertility Parameters

Commencement of luteal activity postpartum (CLA). The heritability of lnCLA was 0.16 (SE 0.05; $P < 0.0005$). There ws no effect of PCH. Additional analyses showed the regressions of lnCLA on PTA for milk, fat, and protein yield (kg), and PIN95 (£) were all unfavorable (1.17×10^{-4} SE 7.51×10^{-5}, 5.66×10^{-3} SE 2.05×10^{-3}, 4.47×10^{-3} SE 2.63×10^{-3}, and 1.38×10^{-3} SE 7.15×10^{-4}, respectively). While there appeared to be a tendency for cows with a higher genetic merit for production traits to have a longer interval to CLA, the only coefficient that was statistically significant as being different from zero was that for PTA fat yield (kg). The magnitude of the regression was such that for every increase in genetic merit of 10 kg of fat, CLA would increase by 5.8% (approximately 1.5 d).

The geometric means for CLA during the four seasons were 27.1, 28.0, 20.8, and 20.9 d for winter, spring, summer, and autumn, respectively ($P < 0.025$). Specific contrasts showed the interval during spring was longer than in any other season. Cows calving during the spring took 35% longer (approximately 8 d) to commence luteal activity postpartum than those calving in summer. Later lactations (four +) were associated with prolonged CLA ($P < 0.05$). The occurrence of uterine infection also had a significant impact ($P < 0.01$) on lnCLA with animals experiencing uterine infection, requiring 18% (approximately 5 d) longer to commence luteal activity than those that did not. Effects of herd, year, retained placenta, dystocia, and diet were not statistically significant.

Length of the first luteal phase (LUT1). The heritability of lnLUTI was 0.17 (SE 0.06; $P < 0.001$). There was no effect of PCH. Additional analysis showed the regressions of lnLUTI on PTA for milk, fat and protein yield (kg), and PIN95 (£) were all negative in direction (-1.50×10^{-4} SE 8.47×10^{-5}, -3.70×10^{-3} SE -2.30×10^{-3}, -5.74×10^{-3} SE 2.94×10^{-3} and -1.58×10^{-3} SE 7.98×10^{-4}, respectively). Therefore, there was a tendency for animals with higher genetic merit for production traits to have a shorter first luteal phase postpartum, although the only coefficients significantly different from zero were protein yield (kg) and PIN95 (£). The magni-

Table 1. Numbers of records (n), means and phenotypic standard deviations (σ_P).

Trait	Abbrev.	n	Mean	σ_P
Commencement of luteal activity (days; ln)	CLA	1212	3.22	0.52
Length of first luteal phase (days; ln)	LUTI	1146	2.52	0.59
Occurrence of persistent CL type I (0,1)	PCLI	1146	0.17	0.38
Pregnancy to first service (0,1)	PFS	667	0.40	0.48
Interval to first service (days)	IFS	1121	83.66	37.80
Predicted peak milk yield on day 56 (kg)	MY56	1152	32.53	5.40

tude of the regression on PTA protein yield was such that for every 20 kg increase in protein, LUTI decreased by 10.8% (i.e., approximately 2 d). Similarly, for every £20 increase in PIN, LUTI decreased by 3.11% (i.e., approximately 0.5 d).

The first luteal phase of an animal that experienced postpartum uterine infection was extended on average by 17%, or approximately 2 d ($P < 0.005$). There was no statistically significant effect of herd, year, season, retained placenta, dystocia, diet, or lactation number.

Persistent corpus luteum (PCLI). The heritability of PCLI was 0.13 (SE 0.06; $P < 0.05$). Animals experiencing uterine infection were more likely ($P < 0.001$; 20.2 vs. 32.6%) to subsequently suffer from PCLI (i.e., first luteal phase ≥ 19 d; Lamming and Darwash, 1998; Royal et al., 2000a). There was no significant effect of the other factors tested, including PCH.

Analysis of Genetic Variation in Traditional Fertility Parameters

Pregnancy rate to first service (PFS). The heritability of PFS was 0.14 (SE 0.08; $P < 0.05$). Both herd

($P < 0.025$) and diet ($P < 0.01$) had significant effects on PFS. There was no other significant effect on PFS.

Interval to first service (IFS). The heritability of IFS was 0.11 (SE 0.05; $P < 0.025$). Herd ($P < 0.001$), year ($P < 0.01$), diet ($P < 0.001$), and occurrence of uterine infection ($P < 0.05$) had significant effects upon this trait such that this interval was 9.2% longer in animals experiencing uterine infection (112.6 vs 103.7 d). There was no other significant effect on this trait.

Analysis of Genetic Variation in Predicted Milk Yield

Predicted milk yield on d 56 (MY56). The heritability of MY56 was 0.50 (SE 0.06; $P < 0.001$). Interestingly, the effects of PCH only approached significance ($P < 0.1$). Further investigation as a consequence of this result showed that, as expected, a positive relationship between sire PTA for milk yield and PCH was significant ($P < 0.01$), such that for every 10% increase in PCH, PTA milk increased by 91.73 kg. Herd ($P < 0.001$), lactation number ($P < 0.001$), and diet ($P < 0.001$) all had significant effects.

Table 2. Heritabilitites (on the diagonal), genetic (below diagonal), and phenotypic (above diagonal) correlations between traditional and endocrine measurements of fertility and peak milk yield (SE in brackets).

	lnCLA	lnLUTI	PCLI	PFS	IFS	MY56
lnCLA[1]	0.16 (0.05)***	−0.05 (0.03)	−0.08 (0.03)*	−0.03 (0.04)	0.12 (0.03)*	0.05 (0.03)
lnLUTI[2]	−0.44 (0.23)*	0.17 (0.06)***	. . . . . .	0.04 (0.04)	0.08 (0.03)*	−0.01 (0.04)
PCLI[3]	−0.33 (0.27)	. . . . . .	0.13 (0.06)*	0.05 (0.04)	0.08 (0.03)*	0.01 (0.03)
PFS[4]	0.49 (0.47)	0.44 (0.43)	−0.14 (0.46)	0.14 (0.08)*	0.02 (0.05)	−0.04 (0.05)
IFS[5]	−0.03 (0.27)	0.19 (0.29)	0.31 (0.33)	0.35 (0.59)	0.11 (0.05)*	−0.013 (0.03)
MY56[6]	0.36 (0.17)*	−0.51 (0.18)**	−0.31 (0.22)	−0.27 (0.31)	0.32 (0.20)	0.50 (0.06)***

[1]ln commencement of luteal activity postpartum (days).

[2]ln length of first luteal phase postpartum (days).

[3]Persistent CL (0, 1).

[4]Pregnancy to first service (0, 1).

[5]Interval to first service (days).

[6]Estimated milk yield on d 56 postpartum (kg).

*$P < 0.05$.

**$P < 0.01$.

***$P < 0.001$.

Genetic and Phenotypic Correlations

Correlations between endocrine and traditional fertility measures and peak milk yield are presented in Table 2.

Associations among endocrine and traditional fertility traits. Phenotypic associations between the endocrine measures lnCLA, lnLUTI, and PCLI and the traditional measure IFS were all positive and significant (0.12, 0.08, and 0.08; $P < 0.05$). Therefore, interval to first service increased with increasing lnCLA, lnLUTI, and PCLI. All phenotypic correlations between endocrine measures and PFS were below 0.05, and not statistically significant. None of the genetic correlations with PFS and IFS was significant, and the standard errors were large.

The genetic correlation of lnCLA and lnLUTI was negative and statistically significant (–0.44, SE 0.23; $P < 0.05$). Therefore, genetically, cows experiencing a shorter interval to CLA are more likely to experience a longer first luteal phase. The phenotypic correlation was similar in direction, whereas the environmental correlation was positive (0.04). Neither was significantly different from zero.

Associations with MY56. The genetic correlations of MY56 with lnCLA and lnLUTI were both statistically significant. Genetically, cows with high milk yield at d 56 tended to have longer CLA and shorter first luteal phases.

DISCUSSION

A number of genetic parameters have been estimated for fertility and production traits in the current study. The principal findings demonstrate that a substantial proportion of the variation among individual Holstein-Friesian UK dairy cattle in three endocrine fertility traits (lnCLA, lnLUTI, and PCLI) is of an additive genetic nature ($h^2 = 0.16$, 0.17, and 0.13, respectively). In addition, lnCLA and lnLUTI have significant genetic correlations with MY56, which is close to peak yield (r_g ranging from 0.36 to –0.51). Interestingly, PCH of the cow had no significant effect on any of the fertility traits monitored. Therefore, this study provides clear evidence to confirm that endocrine measurements of fertility have substantially higher heritabilities than the values commonly reported for traditional fertility traits ($h^2 < 0.05$) and that significant and strong genetic correlations exist between endocrine fertility traits and production traits.

This study confirms the heritability for lnCLA reported originally by Darwash et al. (1997; 0.21). This is important because the original study (1975 to 1982) was on pure British Friesian dairy cows (n = 2000), and did not include the modern Holstein. In addition, it agrees with the estimates published by Veerkamp et al. (1998, 2000; $h^2 = 0.14$ to 0.20) for a population of Holstein-Friesians in the Netherlands (1994 to 1996). All studies have been either small or very small, and there are benefits from pooling these estimates to get a weighted average. When this is done, the pooled estimate for heritability of lnCLA (n = 3282 lactations) was 0.18 ± 0.03 (SE).

We have shown for the first time that the occurrence of PCLI is heritable, and this offers the possibility of specifically addressing this condition via selection. Although all four atypical milk progesterone patterns identified by Lamming and Darwash (1998; delayed ovulation type I, DOV I; prolonged inter-luteal intervals, DOV II; PCLI and PCLII) affect pregnancy rates to first service, PCLI and PCLII were of particular concern since both conditions had a major phenotypic impact on pregnancy rates (Lamming and Darwash, 1998; Royal et al., 2000a). Royal et al. (2000a) also showed that the incidence of both these conditions has increased phenotypically over the last 20 yr. PCL results from delayed luteolysis: This condition has been reported in cows showing loss of the embryo/conceptus (possibly through mechanisms involving interferon-tau; Thatcher et al., 1995; Darwash et al. 1999; Lamming and Darwash, 1998), congenital anomalies of the uterine horn, and inflammatory and infectious conditions of the uterus (Erb et al., 1985; Lamming and Darwash, 1998). The latter is thought to cause a suboptimal uterine environment that consequently disrupts the normal luteolytic mechanism of the uterus, resulting in a longer CL lifespan (Noakes et al., 1990; Lamming and Darwash, 1998).

The heritability estimated for lnLUTI was 0.17, which is comparable in magnitude to the heritability of lnCLA. While the impact of LUTI on fertility has not been studied in detail as a quantitative trait, an extended luteal phase is a syndrome that is associated with PCLI and PCLII and, consequently, subfertility. In the current analysis, both genetic and phenotypic correlations with IFS were positive. The mean LUTI has increased by almost 4 d over the last 20 yr (Royal et al., 2000a). In cows monitored 20 yr ago, luteal phase length was shorter in the first estrous cycle postpartum (mean of 10.6 d) than in subsequent estrous cycles (14.9 d during the fourth estrous cycle; Darwash et al., 1998). This trend was not evident in the current dairy population, where length of the luteal phase remained approximately 15 d throughout the first four estrous cycles postpartum (Royal et al., 2000a).

Throughout this analysis, estimates of genetic correlations between endocrine and traditional traits of fertility were attempted, but unfortunately it is clear at this stage that our data, despite the inclusion of Roslin

data, are still too few to provide credible estimates. However, the phenotypic relationships between all endocrine traits and IFS were favorable and statistically significant such that IFS increased with increasing CLA, increasing LUTI and the increased occurrence of PCLI. This is in agreement with the principle that early reestablishment of postpartum ovarian activity is an important prerequisite for high fertility (Darwash et al., 1997a), and with research published by Lamming and Darwash (1998), who reported that animals experiencing PCLI (extended LUTI) had reduced fertility as monitored by several different traditional fertility measurements and higher levels of embryo mortality.

The traditional measurements of fertility used here (IFS and PFS) differed from those commonly used to analyze fertility, because they rely on a correctly timed insemination, the subsequent maintenance of high milk progesterone, and on an actual calving rather than on service date records or scanning data alone. This was possible because of the availability of the progesterone data and was carried out to eliminate some of the managerial effects introduced by incorrect service data or services at the wrong time in the estrous cycle. Heritability estimates were high (but with high standard errors) compared with previously published estimates for IFS (0.02 to 0.07; Van Arondonk et al., 1989; Faust et al., 1989; Bagnato and Oltenacu, 1993; Hoekstra et al., 1994; Grosshans et al., 1997; Pryce et al., 1997; Kadarmideen et al., 2000) and PFS (0.01 to 0.05; Faust et al., 1989; Oltenacu et al., 1991; Weller and Ron, 1992; Bagnato and Oltenacu, 1993; Boichard and Manfredi, 1994; Hoekstra et al., 1994; Pryce et al., 1997; Kadarmideen et al., 2000). This is most likely due to the small size of the current database and the removal of a proportion of the environmental variation though use of milk progesterone profiles.

To investigate various correlations between milk yield and fertility, it seemed more relevant to use milk yield when it was approaching the period of peak yield, when energy balance is at its nadir, and close to the time when insemination decisions are being taken. This suggestion is in agreement with Philipsson (1981), who argued that production levels beyond 7 mo postpartum are irrelevant since cows may well be at different stages of gestation. Genetic selection for milk yield on average results in a more severe negative energy balance (r_g = between –0.05 to –0.91; Veerkamp, 1998). Furthermore, the phenotypic, environmental, (Butler et al., 1981; Butler and Smith, 1989; Canfield and Butler, 1990; Villa-Godoy et al., 1990; DeRouen et al., 1994; Beam and Butler, 1998) and genetic relationships (Veerkamp et al., 2000) between energy balance and fertility are all unfavorable. The heritability estimate for MY56 (which is not strictly a test-day milk yield estimation) using a Wood's curve (Wood, 1967) with random regressions for cows and lactations within cows was 0.50. This agrees with estimates for test-day milk yields published by Jamrozik and Schaeffer (1997), which were between 0.40 and 0.59 for daily milk yield. However, it is higher than the figures reported by Jamrozik et al., (1997; 0.38 to 0.40), Pander et al. (1992; 0.34), and Brotherstone et al. (2000; 0.10 to 0.25). This may reflect the removal of environmental variation by the random regression model used to predict MY56 in the current study.

There was clear evidence of a positive genetic association between MY56 and lnCLA. When PTA were used as regression covariates, increases in all yield traits increased lnCLA. Since the logarithmic scale is multiplicative, the increase in CLA (expressed in days) per unit increase in PTA milk yield is predicted to be greater at high yields than at lower yields. Therefore, this positive genetic association may be an underlying endocrine factor in the observed decrease in fertility associated with the genetic increase in milk yield. The genetic correlation between MY56 and lnCLA was 0.36 (se 0.17; $P < 0.05$). This is compared to 0.51 (SE 0.3; NS) obtained by Veerkamp et al. (2000) for 305-d milk yield and CLA. A pooled estimate of the two results, albeit the two use slightly different measures of milk yield, gives an estimate of 0.40 (SE 0.15). This estimate is similar in magnitude to genetic correlations between traditional fertility traits and milk yield (range = 0.16 to 0.64 for calving interval, days to first service and days open with milk yield; Van Arondonk et al., 1989; Bagnato and Oltenacu, 1993; Campos et al., 1994; Hoekstra et al., 1994; Grosshans et al., 1997; Kadarmideen et al., 2000; Pryce et al., 2000) which are all unfavorable. However, it is likely that the estimates between milk yield and endocrine measurements are less open to bias since they are not as open to the confounding effects of management decisions. For instance, since insemination in high yielding cows is often delayed, genetic variance is likely to be exaggerated, which may affect any estimated correlations.

Although these genetic correlations are unfavorable, they are not 1, and this does not, therefore, imply that fertility (or CLA in this case) will decline inevitably as genetic progress occurs in milk yield. However, as discussed by Darwash et al. (1999), it does imply that without promotion or maintenance of genetic merit for CLA, fertility is likely to decline. Furthermore, the unfavorable correlation does not prevent good management from producing both high fertility and high yields, but it will become increasingly difficult in the long term to maintain the current standards if nothing positive is done to include fertility in a selection index. This supports earlier publications by Pryce et al. (1997, 1998), Dematawewa and Berger (1998), Linde and Phil-

ipsson (1998), Vandorp et al. (1998), and Kadarmideen et al. (2000). It is important also to state that just because an unfavorable genetic correlation has been observed between CLA and milk yield, not all measures of fertility will have the same or even a similar correlation. In fact, the genetic associations between MY56 and lnLUTI and PCLI were negative in direction. This was observed both in the genetic regressions and in the genetic correlation estimates. This is an interesting finding because although milk yield has genetically and phenotypically increased over the last 20 yr through selection, LUTI or PCLI have phenotypically increased in length and in incidence, respectively, over the same period. However, in both cases the environmental correlations were positive and significant (0.22, $P < 0.005$ and 0.14, $P < 0.05$, respectively). This may be a prime example of how it is possible for managerial and environmental influences to conceal the true genetic relationships. Realistically, it is impossible to finally resolve these issues until more precise correlations and better data are available for analysis.

It has frequently been suggested that the breed replacement of the European Friesian by the North American Holstein may explain a proportion of the decline seen in fertility. Support for this hypothesis was given by Hoekstra et al. (1994), where regression on percentage Holstein explained a decline of approximately 8% in nonreturn rate (56 d postinsemination) and pregnancy to first service. This suggested that the introduction of Holstein genes had decreased the performance of the Dutch dairy herd, and that the decline will continue until the process of genetic replacement is complete. However, the regression of lnCLA on PCH in the current analyses predicted only a small increase in lnCLA as a result of substitution of the Friesian by the Holstein. This is consistent with the fact that mean CLA has not changed phenotypically since the 1975 to 1982 study of Darwash et al. (1997a) on British Friesians (Royal et al., 2000a).

Analysis of PCH and the effect of MY56 present a paradox since the introduction of the Holstein has resulted in an increase in milk yield. (It is important to note that the database included cows with a wide range of Holstein genes, from 0 to 100%; Figure 1). This paradox is resolvable, however, and in resolving it one should note that the associations with yield were estimated after accounting for the percentage Holstein. The Holstein and the Friesian, though clearly from a common gene pool, have been genetically separated for 12 generations, and subjected to different and changeable selection pressures over the intervening period. For reasons of genetic drift, there is no reason to assume that a Holstein and a Friesian with the same genetic merit for yield will have the same CLA, even though both

these populations may display a positive genetic association between yield and CLA. Other reasons may be advanced, but this argument shows that the results of the current study are not in contradiction.

The apparent lack of impact of percentage Holstein on the lnLUTI or PCLI is also a curious finding, bearing in mind the dramatic increase in this syndrome since 1975 to 1982. However, our data structure and analyses do not cover all genetic scenarios that may be operating. For example, if there was a locus with a dominant allele coming from the Holstein, increasing the likelihood of PCLI, then it is likely that the power in our study would be limited with few pure Friesians, and much of the information arising from Holstein percentages from 50 to 100% upgraded population.

As expected, PTA for production traits correlated strongly with percentage Holstein, so it was surprising that CLA was related to yield but not percentage Holstein. The Friesians and low-percentage Holsteins included in the study had low PTA for yield, so they had not been selected for high yield. One possible explanation for this inconsistency is that the Friesians monitored were managed to result in a high yield (i.e., were performing above their PTA). A second explanation is that environmental improvements have masked the genetic trend in CLA expected to result from the introduction of Holstein genes into the UK herd. Even if the latter suggestion were true, however, it should be noted that because of the genetic relationship between yield and fertility, environmental improvements will not overcome this trend in the future.

Pregnancy to first service was not affected by uterine infection because insemination was delayed in infected cows until after the infection was eliminated. However, uterine infection did affect interval to first service and the three endocrine fertility parameters investigated, probably because they are influenced by events immediately postpartum. These results highlight the need for early identification and treatment of uterine infection postpartum and for a better understanding of the mechanisms underlying it.

CONCLUSIONS

This study has shown that several aspects of the progesterone profile are heritable, in addition to the interval to CLA. This finding, coupled with the potential of online milk progesterone monitoring, gives a much broader perspective to the active and sustained improvement of reproductive health and performance of dairy cattle, through the application of well-established genetic principles. The data presented are small in number; however, the findings considerably improve

the knowledge of genetic correlation with milk yield. Progress is made with better information.

REFERENCES

Bagnato, A., and P. A. Oltenacu. 1993. Genetic studies of fertility traits and production in different parities in Italian Friesian cattle. J. Anim. Br. Genet. 110:126–134.

Beam, S. W., and W. R. Butler. 1998. Energy balance, metabolic hormones, and early postpartum follicular development in dairy cows fed prilled lipid. J. Dairy Sci. 81:121–131.

Beam, S. W., and W. R. Butler. 1999. Energy balance effects on follicular development and first ovulation in post-partum cows. J. Reprod. Fertil. 54:411–424.

Boichard, D., and F. Manfedi. 1994. Genetic analysis of conception rate in French Holstein cattle. Acta Agric. Scand. 44:138–145.

Brotherstone, S., I. M. S. White, and K. Meyer. 2000. Genetic modelling of daily milk yield using orthogonal polynomials and parametric curves. Anim. Sci. 70:407–415.

Butler, W. R., R. W. Everett, and C. E. Coppock. 1981. The relationships between energy balance, milk production, and ovulation in postpartum Holstein cows. J. Anim. Sci. 53:742–748.

Butler, W. R., and R. D. Smith. 1989. Interrelationships between energy balance and post-partum reproductive function in dairy cattle. J. Dairy Sci. 72:767–783.

Campos, M. S., C. J. Wilcox, C. M. Beceril, and A. Diz. 1994. Genetic parameters for yield and reproductive traits of Holstein and Jersey cattle in Florida. J. Dairy Sci. 77:867–873.

Canfield, R. W., and W. R. Butler. 1990. Energy balance and pulsatile LH secretion in early postpartum dairy cattle. Domest. Anim. Endocrinol. 7:323–330.

Darwash, A. O., G. E. Lamming, and J. A. Woolliams. 1997a. The phenotypic association between the interval to postpartum ovulation and traditional measures of fertility in dairy cattle. Anim. Sci. 65:9–16.

Darwash, A. O., G. E. Lamming, and J. A. Woolliams. 1997b. Estimation of genetic variation in the interval from calving to postpartum ovulation of dairy cows. J. Dairy Sci. 80:1227–1234.

Darwash, A. O., G. E. Lamming, and J. A. Woolliams. 1998. Identifying heritable endocrine parameters associated with fertility in postpartum dairy cows. Proceedings of the International Workshop on Genetic Improvement of Functional Traits in Cattle; Fertility and Reproduction, GRUB, Germany, November 23–25, 1997. Interbull. 18:40–54.

Darwash, A. O., G. E. Lamming, and J. A. Woolliams. 1999. The potential for identifying heritable endocrine parameters associated with fertility in postpartum dairy cows. Anim. Sci. 68:333–347.

Dematawewa, C. M. B., and P. J. Berger. 1998. Genetic and phenotypic parameters for 305-day yield, fertility, and survival in Holsteins. J. Dairy Sci. 81:2700–2709.

DeRouen, S. M., D. E. Franke, D. G. Morrison, W. E. Yatt, D. F. Coombs, T. W. White, P. E. Humes, and B. B. Greene. 1994. Prepartum body condition and weight influences on reproductive performance of first-calf beef cows. J. Anim. Sci. 72:1119–1125.

Erb, H. N., R. D. Smith, P. A. Oltenacu, C. L. Guard, R. B. Hillman, P. A. Powers, M. C. Smith, and M. E. White. 1985. Path model of reproductive disorders and performance, milk fever, mastitis, milk yield, and culling in Holstein cows. J. Dairy Sci. 68:3337–3349.

Faust, M. A., B. T. McDaniel, and O. W. Robinson. 1989. Genetics of reproduction in primiparous Holsteins. J. Dairy Sci. 72:194–201.

Grosshans, T., Z. Z. Xu, L. J. Burton, D. L. Johnson, and K. L. MacMillan. 1997. Performance and genetic parameters for fertility of seasonal dairy cows in New Zealand. Livest. Prod. Sci. 51:41–51.

Hoekstra, J., A. W. Van der Lugt, J. H. J. Van der Werf, and W. Ouweljes. 1994. Genetic and phenotypic parameters for milk production and fertility traits in upgraded dairy cattle. Livest. Prod. Sci. 40:225–232.

Jamrozik, J., and L. R. Schaeffer. 1997. Estimates of genetic parameters for a test day model with random regressions for yield traits of first lactation Holsteins. J. Dairy Sci. 80:762–770.

Jamrozik, J., L. R. Schaeffer, Z. Liuand, and G. Jansen. 1997. Multiple trait random regression test day model for production traits. Proceedings of the Interbull meeting, Vienna, Austria.

Kadarmideen, H. N., R. Thompson, and G. Simm. 2000. Linear and threshold genetic parameters for disease, fertility, and milk production in dairy cattle. Anim. Sci. 71:411–419.

Lamming, G. E., and A. O. Darwash. 1998. The use of milk progesterone profiles to characterize components of subfertility in milked dairy cows. Anim. Reprod. Sci. 52:175–190.

Lawes Agricultural Trust. 1997. Genstat 5, Release 4.1. Third Edition. IACR Rothamstead.

Lindé, B., and J. Philipsson. 1998. Genetic correlations between production with disease resistance and fertility in dairy cattle and consequences for total merit selection. Acta Agric. Scand. 48:216–221.

Lindé, B., and J. Philipsson. 2001. The Scandinavian experience of including fertility in breeding programmes. British Society of Animal Science Occasional Publication. BSAS. Galway, Ireland.

Noakes, D. E., L. M. Wallace, and G. R. Smith. 1990. Pyometra in a Friesian heifer: bacteriological and endometrial changes. Vet. Rec. 126:509.

Oltenacu, P. A., A. Frick, and B. Lindhe. 1991. Relationship of fertility to milk yield in Swedish cattle. J. Dairy Sci. 74:264–268.

Royal, M. D., A. O. Darwash, A. P. F. Flint, R. Webb, J. A. Woolliams, and G. E. Lamming. 2000a. Declining fertility in dairy cattle: changes in traditional and endocrine parameters of fertility. Anim. Sci. 70:487–501.

Royal, M. D., J. A. Woolliams, R. Webb, and A. P. F. Flint. 2000b. Estimation of genetic variation in the interval from parturition to commencement of luteal activity in Holstein-Friesian dairy cows. Proc. J. Reprod. Fertil. Series 25 (Abstr. 74).

Royal, M. D., G. E. Mann, and A. P. F. Flint. 2000c. Strategies for reversing the trend towards subfertility in dairy cattle. Vet. J. 160:53–60.

Pander, B. L., W. G. Hill, and R. Thompson. 1992. Genetic parameters of test day records of British Holstein-Friesian heifers. Anim. Prod. 55:11–21.

Philipsson, J. 1981. Genetic aspects of female fertility in dairy cattle. Livest. Prod. Sci. 8:307–319.

Pryce, J. E., R. F. Veerkamp, R. Thompson, W. G. Hill, and G. Simm. 1997. Genetic aspects of common health disorders and measures of fertility in Holstein-Friesian dairy cattle. Anim. Sci. 65:353–360.

Pryce, J. E., R. J. Esslemont, R. Thompson, R. F. Veerkamp, M. A. Kossaibati, and G. Simm. 1998. Estimation of genetic parame-

ters using health, fertility, and production data from a management recording system for dairy cattle. Anim. Sci. 66:577–584.

Pryce, J. E., M. P. Coffey, and S. Brotherstone. 2000. The genetic relationship between calving interval, condition score, and linear type and management traits in registered Holsteins. J. Dairy Sci. 83:2664–2671.

Thatcher, W. W., M. D. Meyer, and G. Danet-Desnoyers. 1995. Maternal recognition of pregnancy. J. Reprod. Fertil. 49:15–28.

Van Arondonk, J. A. M., R. Hovenier, and W. De Boer. 1989. Phenotypic and genetic association between fertility and production in dairy cows. Livest. Prod. Sci. 21:1–12.

Vandorp, T. E., J. C. M. Dekkers, S. W. Martin, and J. P. T. M. Noordhuizen. 1998. Genetic parameters of health disorders, and relationships with 305-day milk yield and conformation traits of registered Holstein cows. J. Dairy Sci. 81:2264–2270.

Veerkamp, R. F. 1998. Selection for economic efficiency of dairy cattle using information on live weight and feed intake: A review. J. Dairy Sci. 81:1109–1119.

Veerkamp, R. F., J. K. Oldenbroek, and T. Van der Lende. 1998. The use of milk progesterone measurements for genetic improvement of fertility traits in dairy cattle. Proceedings of the International Workshop on Genetic Improvement of Functional Traits in Cattle; Fertility and Reproduction, GRUB, Germany, November 23–25, 1997. Interbull. 18:62–65.

Veerkamp, R. F., J. K. Oldenbroek, H. J. Van der Gaast, and J. H. J. Van der Werf. 2000. Genetic correlation between days until start of luteal activity and milk yield, energy balance, and live weight. J. Dairy Sci. 83: 577–583.

Villa-Godoy, A., T. L. Hughes, R. S. Emery, W. J. Enright, A. D. Ealy, S. A. Zinn, and R. L. Fogwell. 1990. Energy balance and body condition influences luteal function in Holstein heifers. Domest. Anim. Endocrinol. 7:135–148.

Weller, J. I., and M. Ron. 1992. Genetic analysis of fertility traits in Israeli Holsteins by linear and threshold models. J. Dairy Sci. 75:2541–2548.

Wood, P. D. P. 1967. Algebraic model of the lactation curve in cattle. Nature (Lond). 216:164–165.

APPENDIX

The initial statistical model used to investigate the trait Y for cow u was:

$$Y_{mnopqrstu} = \mu + A_m + B_n + C_o + D_p + E_q$$
$$+ F_r + G_s + b_1 H_u + BC_{no} + CD_{op} + BD_{np}$$
$$+ BCD_{nop} + I_t + J_u + K_u + L_{mnopqrstu}$$

$Y_{mnopqrstuv}$ = variable with effects as follows:

μ = overall mean,

A_m = fixed effect of lactation number ($m = 1$–9),

B_n = fixed effect of herd ($n = 1$–9),

C_o = fixed effect of year ($o = 1995$–1998),

D_p = fixed effect of season ($p = 1$–4),

E_q = fixed effect of uterine infection postpartum ($q = 1$–2),

F_r = fixed effect of retained placenta ($r = 1$–2),

G_s = fixed effect of dystocia ($s = 1$–2),

$b_1 H_u$ = regression on percentage Holstein genes with coefficient b_1 (denoted as PCH of cow in text),

I_t = fixed effect of diet ($t = 1$–23),

BC_{no} = random effect of herd-year interaction,

CD_{op} = random effect of year-season interaction,

BD_{np} = random effect of herd-season interaction,

BCD_{nop} = random effect of herd-year-season interaction,

J_u = random effect of breeding value (N (0, σ^2_AA)) where A is the numerator, relationship matrix of the cows derived from the relationships available in the data,

K_u = random effect of the individual (N (0, σ^2_c)) and

$L_{mnopqrstuv}$ = random error term (N (0, σ^2_e))