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Genetic analysis of atypical progesterone profiles in Holstein-Friesian cows from experimental research herds

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ABSTRACT

The objective of this study was to quantify the genetic variation in normal and atypical progesterone profiles and investigate if this information could be useful in an improved genetic evaluation for fertility for dairy cows. The phenotypes derived from normal profiles included cycle length traits, including commencement of luteal activity (C-LA), interluteal interval, luteal phase length, and interovulatory interval. In total, 44,977 progesterone test-day records were available from 1,612 lactations on 1,122 primiparous and multiparous Holstein-Friesian cows from Ireland, the Netherlands, Sweden, and the United Kingdom. The atypical progesterone profiles studied were delayed cyclicity, prolonged luteal phase, and cessation of cyclicity. Variance components for the atypical progesterone profiles were estimated using a sire linear mixed model, whereas an animal linear mixed model was used to estimate variance components for the cycle length traits. Heritability was moderate for delayed cyclicity (0.24 ± 0.05) and C-LA (0.18 ± 0.04) but low for prolonged luteal phase (0.02 ± 0.04), luteal phase length (0.08 ± 0.05), interluteal interval (0.08 ± 0.14), and interovulatory interval (0.03 ± 0.04). No genetic variation was detected for cessation of cyclicity. Commencement of luteal activity, luteal phase length, and interovulatory interval were moderately to strongly genetically correlated with days from calving to first service (0.35 ± 0.12 , 0.25 ± 0.14 , and 0.76 ± 0.24 , respectively). Delayed cyclicity and C-LA are traits that can be important in both genetic evaluations and management of fertility to detect (earlier) cows at risk of compromised fertility. Delayed cyclicity and C-LA were both strongly genetically correlated with milk yield in early lactation (0.57 ± 0.14 and 0.45 ± 0.09 , respectively), which may

imply deterioration in these traits with selection for greater milk yield without cognizance of other traits.

Key words: dairy cow, progesterone profile, fertility, genetic parameter

INTRODUCTION

Good reproductive performance is important for both economic and ethical reasons; for example, cow welfare and consumer preferences (Berglund, 2008). Reproductive performance affects milk production, breeding costs, and both voluntary and involuntary culling, all of which affect the profitability of a dairy herd (Plazier et al., 1997). Female fertility in dairy cows has deteriorated for several decades, although this decline has now been halted in most populations (e.g., Philipsson, 2011). Suboptimal fertility has been reported worldwide in many dairy populations, particularly in Holstein-Friesian (HF) populations subjected to strong genetic selection for milk production (Rodriguez-Martinez et al., 2008). Reproductive and management factors contributing to the deterioration in the overall fertility phenotype may include poor return to cycling postpartum, poor expression of estrus, as well as inappropriate timing of insemination (Friggens and Chagunda, 2005; Crowe, 2008; Walsh et al., 2011). Dobson et al. (2008) documented that the percentage of animals that stand to be mounted and the duration of standing heat have decreased during the last 30 to 50 yr, whereas the number of silent heats has increased with increasing milk production.

An estrus cycle, which averages 21 d (range 18–24 d), is defined as the period initiated by an increase in progesterone (P₄) above a threshold value and subsequently terminated with the next decrease below the threshold P₄ value. The estrus cycle constitutes 3 phases: (1) the onset of the estrus cycle, (2) the follicular phase, and (3) the luteal phase (Friggens and Chagunda, 2005). To obtain a 1-yr calving interval, cow cyclicity should resume at least 60 d postpartum (Walsh et al., 2011). Early resumption of ovarian cyclicity postpartum facilitates a greater number of estrus

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cycles before insemination which, on average, increases the likelihood of subsequent conception (Darwash et al., 1997a). Relative to multiparous cows, primiparous cows have, on average, a greater incidence of delayed interval postpartum to first ovulation (Tanaka et al., 2008). Opsomer et al. (2000) documented a greater increase in delayed resumption of ovarian activity and more prolonged luteal phases in cows with clinical endometritis. Royal et al. (2002a) reported that cows with a genetically longer interval to the start of the first cycle; that is, commencement of luteal activity (**C-LA**), had a longer calving to first service interval (**CFS**) and a longer calving interval (**CInt**). A later start of ovulation and longer CFS and CInt will likely decrease the total milk production per cow and herd profitability.

Because of the low heritability of traditional fertility measurements (e.g., calving interval, nonreturn rates, conception rates) in dairy cows (Veerkamp et al., 1998), achieving rapid genetic gain for fertility can be difficult. A likely contributing factor to the low fertility traits is environmental effects (e.g., voluntary waiting period, poor heat detection) not properly accounted for in the statistical methods. Therefore, using more detailed phenotypes based on the biology of the animal itself, less prone to random environmental influences, may result in improved heritability estimates and, if genetically correlated with fertility traits in national breeding goals, could be used to increase genetic gain. Moreover, some of these detailed phenotypes may themselves have economic values.

Endocrine fertility traits, including P4-based fertility measures such as C-LA, can offer a more objective and accurate measurement of the ovarian activity in dairy cows (Petersson et al., 2006a) with 3 to 4 times higher heritability than traditional fertility measures (Petersson et al., 2006a; Berry et al., 2012). To obtain reliable measures of P4 profiles, frequent collection of individual cow P4 information is required. A limiting factor is the high cost of collecting P4 data from individual animals (Berry et al., 2012). Recently developed automated inline tools for progesterone sampling and analysis, such as Herd Navigator (DeLaval, Tumba, Sweden) can predict the reproductive status of a cow and can also handle vast amounts of data (Friggens and Chagunda, 2005). These tools may have the potential to be more cost effective for producers replacing the manual collecting of P4 information.

Deviations from a normal estrus cycle, termed atypical P4 profiles, have been associated with compromised fertility (Bulman and Wood, 1980; Royal et al., 2002a). Reduced pregnancy rate in dairy cows has been associated with repeated atypical P4 profiles (Royal et al., 2000). McCoy et al. (2006) showed that any atypical P4 profile delayed CFS and calving interval compared with

normal P4 profiles. Finally, atypical P4 profiles were reported to be a major contributing factor to reduced conception rate (Darwash et al., 1998).

The incidence of atypical P4 profiles has increased in recent years which could be due to, for example, an increased proportion of delayed cyclicity (Royal et al., 2000; Petersson et al., 2006a). In earlier studies, Opsomer et al. (1999) reported that the most common atypical P4 profiles were delayed cyclicity and prolonged luteal phase, which together constituted 21.5% of all profiles and 88% of all atypical P4 profiles, whereas cessation of cyclicity was much less common. Factors reported to be associated with type of profile by Petersson et al. (2006a) include calving season, calving year group, parity, milk production, and BCS. Severe negative energy balance after calving in first-lactation cows can cause a later onset of the ovulation (Petersson et al., 2006b).

Few studies documented the genetic variation in P4-based measures of fertility such as C-LA (Royal et al., 2002b; Petersson et al., 2007; Berry et al., 2012), but to our knowledge there are no studies of the genetic variation in other measures describing normal and atypical P4 profiles, with the exception of Royal et al. (2002a), who reported a heritability estimate for prolonged luteal phase in the first postpartum estrus cycle. The objective of this study, therefore, was to estimate genetic parameters for measures of normal and atypical P4 profiles in HF cows and to investigate if this information could be useful to improve genetic evaluations for fertility.

MATERIALS AND METHODS

Animals

Data were collected from 4 research herds in 4 countries: (1) Jälla, Swedish University of Agricultural Sciences (Sweden) between 1987 and 2011; (2) Teagasc, Moorepark (Ireland) between 2001 and 2004; (3) Scotland's Rural College (United Kingdom; **UK**) between 2003 and 2005; and (4) Wageningen UR Livestock Research (the Netherlands) between 1991 and 1998, and 2003 and 2004. Detailed management information on each of the herds are provided elsewhere (Petersson et al., 2006a; Horan et al., 2005; Pollott and Coffey, 2008; and Veerkamp et al., 2000, respectively).

Across populations, phenotypic data were available from 1,618 lactations from 1,126 primiparous and multiparous HF cows. The cows were in their first to sixth lactation. Table 1 summarizes the information available from each of the 4 research herds.

Cows were coded as pregnant at first service if they had (1) no second service, (2) were not diagnosed as

Table 1. Summary statistics of cows, progesterone (P4) sampling, and milk production for Holstein-Friesian cows in Ireland (IRE), the Netherlands (NDL), Sweden (SWE), and United Kingdom (UK) after editing

Item	IRE	NDL	SWE	UK
Number of cows	168	666	224	148
Number of lactations	280	672	428	238
Parities	1–4	1, 2	1–6	1–5
Number of profiles	287	672	438	240
Number of P4 analyses per week	3	2	2(1) ¹	3
Total number of P4 analyses	9,829	17,216	9,944	7,988
Mean kg of ECM during the first 60 DIM	1,266	1,912	1,876	1,306

¹Two test-days per week until first ovarian cyclical activity was detected; sampling then reduced to once weekly.

“not pregnant” by transrectal ultrasound, or (3) if the number of days from first service to next calving was between 265 and 300 d.

Milk Sampling

In Sweden and the Netherlands, milk samples for progesterone were collected and analyzed twice weekly. After ovarian cyclical activity was detected, sampling in the Swedish herd was reduced to once weekly until first AI. In the Netherlands, P4 was sampled and analyzed twice weekly for the first 100 d of lactation. In both Ireland and the UK, milk was sampled and analyzed 3 times per week until 26 d after first AI in Ireland and until the first 140 d in lactation in UK. The progesterone concentration was determined in whole milk in all 4 populations. In Sweden, 4 different kits were used to determine P4 concentrations. From the start of the collection of data until 1995, the Farmose kit (Orion Diagnostica, Espoo, Finland) was used; between the years 1995 to 1998, the Spectra kit (Orion Diagnostica) was used; and from 1998 to the start of December 2007 the Coat-A-Count kit (Diagnostic Products Corporation, Los Angeles, CA) was used. From December 2007, a Ridgeway kit was used (Ridgeway Science Ltd., Alvington, UK). The threshold values for the luteal phase, which is the period where the corpus luteum secretes high progesterone, for these kits were 25.4, 9.5, 4.1 and 5.0 ng/mL, respectively. In Ireland, the Netherlands, and the UK, milk P4 concentration was determined by using the Ridgeway kit, and the threshold value for the luteal phase was 3 ng/mL. Sampling procedures and more detailed information about the analysis have been described in Petersson et al. (2006a), Horan et al. (2005), Pollott and Coffey (2008), and Veerkamp et al. (2000). In the present study, data on milk yield and milk composition were used to calculate kilograms of ECM (Sjaunja et al., 1990) produced during the first 60 DIM.

P4-Based Fertility Traits as a Measure of Cyclicity

The generated P4 profiles were used to derive early P4-based fertility measurements. Progesterone concen-

trations were plotted using SAS software (version 9.2; SAS Institute, 2012) against days postpartum to first service to establish individual profiles. These were used in the pre-editing of the data. The P4 profiles were classified into 4 categories (Figure 1) based on a modified definition given by Opsomer et al. (2000) and Petersson et al. (2006a). These 4 categories included (1) a normal profile, (2) delayed cyclicity, (3) prolonged luteal phase, and (4) cessation of cyclicity. A normal profile was defined as a first increase in P4 concentration before d 56 postpartum, followed by regular cyclicity as defined by 2 wk of high P4 concentrations (above the threshold for luteal phase) followed by approximately 1 wk of low P4 concentration (below the threshold for luteal phase; Opsomer et al., 1998). Delayed cyclicity was defined as P4 concentrations below the predefined P4 threshold for more than 56 d postpartum followed by a normal cycle. Prolonged luteal phase was defined as a normal start of cyclicity but with high P4 levels, >8 ng/mL, for at least 20 d, followed by a normal cycle. Cessation of cyclicity was defined as a normal start of cyclicity but interrupted for at least 14 d, with P4 concentrations below the P4 threshold value, followed by a normal cycle (Petersson et al., 2006a). Double classifications of atypical profiles occurred in 25 lactations. Profiles with double classification were kept in their respective classes as no difference was found in the results when they were included or excluded in their respective classifications.

Profiles were excluded if the sampling scheme was not followed; that is, the interval between 2 consecutive samples was greater than 10 d before first AI for Sweden and UK and greater than 7 d for the Netherlands and Ireland. In total, 147 lactations were excluded for this reason (77 from Sweden, 13 from the Netherlands, 57 from Ireland, and 0 from UK).

To characterize the P4 profiles, the exact start and end dates of each cycle were determined by linear interpolation between 2 consecutive samples on each side of the P4 threshold value. To be defined as one estrus cycle, at least 2 consecutive P4 values above the threshold had to exist, or 1 P4 value above the P4 threshold

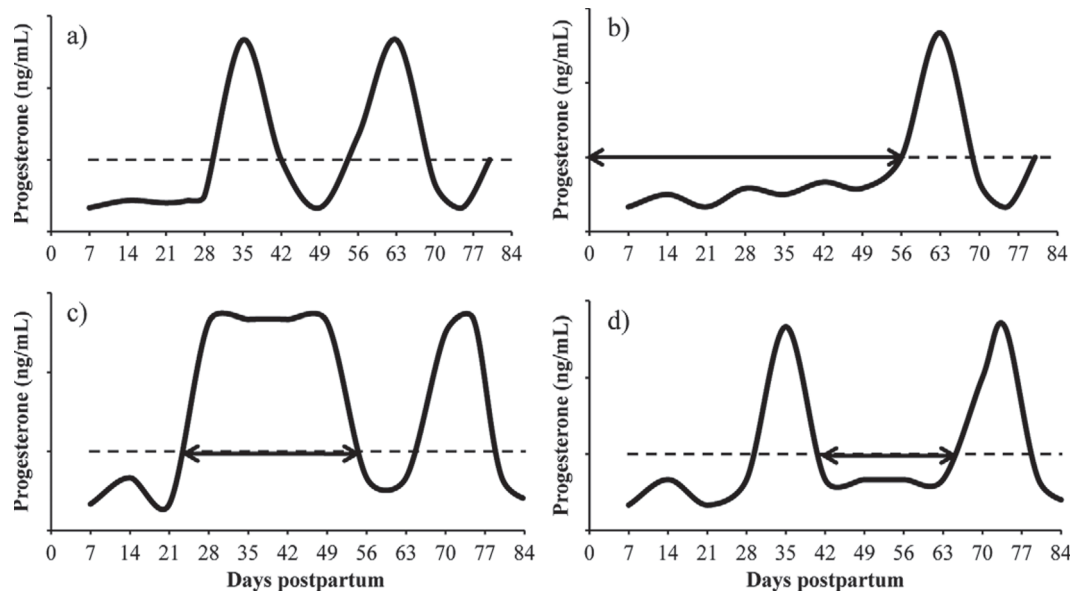


Figure 1. Illustration of the 4 categories of progesterone profiles: (a) normal profile, (b) delayed cyclicality, (c) prolonged luteal phase, and (d) cessation of cyclicality. The solid lines represent the progesterone (P4) level, the dotted line represents the threshold for luteal phase, and the arrows represent the atypical pattern.

and at least 18 d between the 2 closest P4 values. For Sweden and the Netherlands, a limit for prolonged profile was used to account for the few P4 samplings per week. If the first P4 value above the threshold was followed by 2 consecutive lower P4 values and then by 1 higher P4 value above the threshold, it was classified as a normal profile instead of a prolonged luteal phase.

Each normal profile was divided into 4 phases named cycle length traits (Figure 2). These traits included C-LA, interluteal interval (ILI), luteal phase length (LPL), and interovulatory interval (IOI). Commencement of luteal activity was defined as days from calving to the first time the P4 value crossed the threshold for luteal phase. To be included in the analysis, the profiles had to include 1 C-LA measure and at least 2 P4 values after the C-LA. Interluteal interval was defined as the period of time following ovulation in which the corpus luteum secretes progesterone below the P4 threshold, and LPL was measured from the time P4 increases above the threshold value to the time when P4 diminished below the threshold. Interovulatory interval, also known as the estrus cycle length, was defined as the interval between the increase in P4 in one estrus cycle to the P4 increase in the next estrus cycle (Figure 2). Interovulatory intervals were categorized as short (<18 d), normal (18–24 d), and long cycles (>24 d; Royal et al., 2000) and IOI records <5 d were discarded. Luteal phase lengths <4 d were set to 4 d, and ILI <1 d were set to 1 d. Luteal phase lengths >73.5 d and ILI >21.6 d were excluded; 20 lactations were excluded for either of these 2 reasons.

Records of calving data, services, heat observations and pregnancy diagnosis were used to calculate traditional fertility measures including calving to first observed heat (CFH; $n = 732$), CFS ($n = 1,096$), pregnancy to first service (PFS; $n = 1,445$), interval from first to last service (IFLS; $n = 660$), and CInt ($n = 715$).

In total, 35, 99, 102, and 41 unique sires were represented in the Irish, Dutch, Swedish, and UK data sets, respectively. Sweden and the Netherlands had 10 sires in common and the Netherlands and Ireland had 4. Only 1 sire was in common between Sweden and Ireland, Sweden and the UK, and the Netherlands and the UK; Ireland and the UK did not have any sires in common.

Statistical Analysis

A total of 1,612 lactations from 1,122 HF cows from Ireland, the Netherlands, Sweden, and the UK were analyzed for atypical P4 profiles (Table 2). Two lactations from 1 cow were excluded because of missing relatives. A total of 1,618 lactations from 1,126 HF cows from Ireland ($n = 168$), the Netherlands ($n = 586$), Sweden ($n = 224$), and UK ($n = 148$) were analyzed for the cycle length traits. For the atypical P4 profiles, the influence of various fixed and random effects of sire were analyzed with a mixed linear sire model due to the limited data set size. For cycle length traits, the influence of various fixed and random effects of the cow were analyzed with a mixed linear animal model.

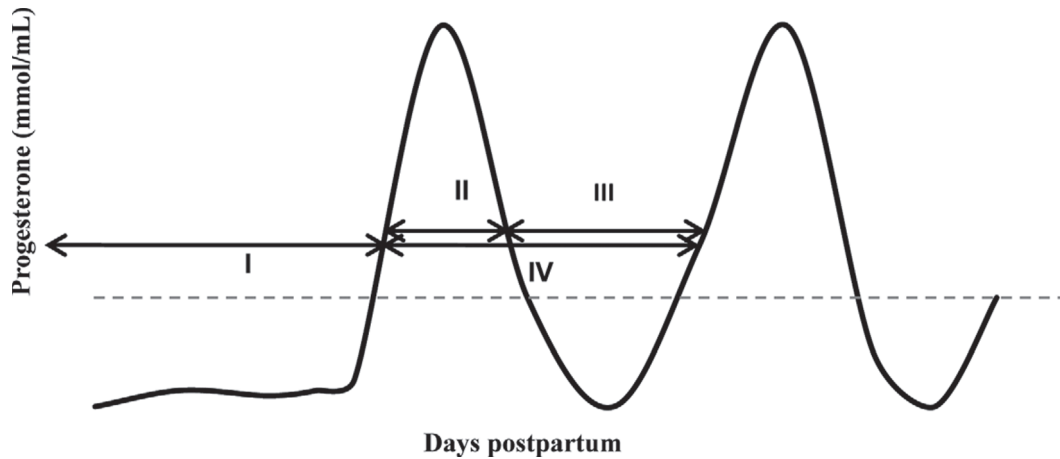


Figure 2. Illustration of the cycle length traits: (I) commencement of luteal activity, (II) luteal phase length, (III) interluteal interval, and (IV) interovulatory interval. The solid lines represent the progesterone (P4) level, the dotted line represents the threshold for luteal phase, and the arrows represent the cycle length traits.

Variance components were estimated with the DMU package (Madsen and Jensen, 2007).

The frequency distributions for the atypical progesterone profiles were normal but the distributions of the cycle length traits were skewed. Therefore, the natural logarithm (**ln**) of C-LA, ILI, LPL, and IOI (i.e., **ln**-CLA, **ln**ILI, **ln**LPL, and **ln**IOI, respectively) was used for these variables as the dependent variables in the statistical models. The models applied were

$$y_{ijklm} = \mu + P_i + Y_j + S_k + \beta_l + e_{ijklm} \text{ and}$$

$$y_{ijklmn} = \mu + P_i + Y_j + S_k + \beta_l + pe_m + e_{ijklmn},$$

where y_{ijklm} was the analyzed trait, μ was the overall mean, P_i was parity within country, Y_j was calving year within country, S_k was calving season within country, and β_l was the cow in the animal model and the sire in the sire model. The permanent environment effect, pe_m , was between lactations of the cow in the sire model and within lactations of the cow in the animal model. For the sire model, the atypical P4 profiles were tested both with and without a permanent environment effect. In the animal model, pe_m between lactations was not used because of partial confounding between the additive

genetic variance and the permanent environment variance. Parity was grouped, within country, into 3 groups for Sweden, Ireland, and the UK (1, 2, and ≥ 3) and into 2 groups for the Netherlands, which only had 2 parities (1 and 2). Calving season was divided into 3 groups for all countries: January–April, May–September, and October–December. Calving years were grouped within country, as follows: Sweden had 6 groups (1987–1993, 1994–1997, 1998–1999, 2000–2003, 2004–2005, and 2006–2011), the Netherlands had 3 groups (1991–1995, 1996–1998, and 2003–2004), Ireland had 3 groups (2001, 2002, and 2003), and the UK had 3 groups (2003, 2004, and 2005). The additive genetic variance (σ_A^2) was estimated utilizing the known pedigree, and the permanent environment effect (σ_{pe}^2) was estimated utilizing the repeated records on cows, in the sire model, over several estrus cycles within lactation and over lactations. Variance components were used to estimate heritability and repeatability. Pedigree information of each animal was tracked back at least 4 generations. The atypical profiles were analyzed first with each one separately and then with all 3 atypical profiles merged together into a single category. Genetic correlations were estimated between the atypical P4 profiles

Table 2. Number of progesterone profiles (prevalence in parentheses¹) in Irish (IRE), Dutch (NLD), Swedish, (SWE), and British (UK) populations

Trait	IRE	NLD	SWE	UK	All
Normal profile	200 (71.4)	487 (73.1)	271 (63.3)	167 (70.2)	1,125 (69.8)
Delayed cyclicity	45 (16.1)	60 (9.0)	51 (11.9)	22 (9.2)	178 (11.0)
Prolonged luteal phase	26 (9.3)	110 (16.5)	83 (19.4)	21 (8.8)	240 (14.9)
Cessation of cyclicity	16 (5.7)	15 (2.3)	33 (7.7)	30 (12.6)	94 (5.8)

¹Twenty-five profiles had 2 types of abnormalities, which were considered when calculating the proportions.

and the traditional fertility measurements (CFH, CFS, PFS, IFLS, and CInt) and kilograms of ECM during the first 60 DIM with a sire model, and for cycle length traits with an animal model using the DMU package (Madsen and Jensen, 2007).

RESULTS

The incidence of normal and atypical P4 profiles per country is summarized in Table 2. A total of 487 profiles (30.2%) were atypical. Table 3 summarizes number of observations, means, and standard deviations (SD) of atypical P4 profiles and cycle length traits. The number of C-LA records was fewer than the number of lactations because of the restrictions imposed on ILI, LPL, and IOI. Mean C-LA for lactations having profiles classified as delayed cyclicity, prolonged luteal phase, and cessation of cyclicity was 70.8 d (SD = 12.5), 24.7 d (SD = 12.2), and 26.0 d (SD = 16.8), respectively.

Normal P4 profiles had a mean IOI of 22.8 d (SD = 10.5) and the incidence of normal, short, and long IOI was 48.5, 20.5, and 31.0%, respectively. First cycles had a mean IOI of 23.9 d (SD = 13.3) with an incidence of a 40.8% normal, 39.7% short, and 29.5% long IOI. Lactations containing a profile with delayed cyclicity had the shortest IOI, with a mean of 20.2 d (SD = 8.6), whereas the IOI for lactations with prolonged luteal phase and cessation of cyclicity were 32.0 d (SD = 12.8) and 32.5 d (SD = 12.5), respectively. Average milk yield during the first 60 DIM was 1,668 kg of ECM.

Parity was associated with delayed cyclicity ($P < 0.01$), ILI ($P < 0.01$), and IOI ($P < 0.01$). The incidence of delayed cyclicity decreased from lactation 1 (12.5%) to lactation 4 (9.4%), as did the incidence of prolonged luteal phase (i.e., from 16.3 to 6.1%). Cessation of cyclicity increased from 4.4% in lactation 1 to 15.2% in lactation 4. Mean LPL across all data was 18.6 d (SD = 10.3) but decreased from 18.8 d in lactation 1 to 16.5 d in lactation 4. Mean ILI across all data was 5.0 d (SD = 3.2), increasing from 4.8 d in lactation 1 to 6.2 d in lactation 4. Interovulatory interval

increased between first (22.8 d) and second (23.8 d) lactation, with no change thereafter. Calving year was associated ($P < 0.01$) with delayed cyclicity, ILI, LPL, and IOI. Calving season was associated with cessation of cyclicity ($P < 0.05$) and ILI ($P < 0.01$). Interluteal interval was shorter in cows calving during the summer and we detected a tendency for a shorter LPL in cows calving in the spring compared with summer- and fall-calving cows.

Cows with delayed cyclicity had a 12-d-longer CFH ($P < 0.01$) than cows with normal profiles, and calving to first service was longer for cows having any atypical P4 profile ($P < 0.01$). Calving to first heat and CFS were 13 and 27 d longer, respectively, for cows with more than one atypical P4 profile. Neither normal nor atypical P4 profiles had any significant association with PFS or IFLS.

Heritability estimates (Table 4) were moderate for delayed cyclicity (0.24) and lnCLA (0.18), and ranged from 0.00 to 0.08 for prolonged luteal phase, cessation of cyclicity, lnILI, lnLPL, and lnIOI. The heritability of whether or not the profile was atypical was 0.04. Similar heritability estimates were obtained when only one record per animal was retained in the analysis (results not shown).

Genetic correlations between type of atypical P4 profiles and type of estrus length traits with more traditional fertility measurements (CFH, CFS, PFS, IFLS, and CInt) and kilograms of ECM during the first 60 DIM are given in Table 5. Standard errors of the estimates were large, with some exceptions. Interovulatory interval was strongly genetically correlated (0.76 ± 0.24) with calving to first service, whereas lnLPL and lnCLA were both moderately genetically correlated (0.25 ± 0.14 and 0.35 ± 0.12 , respectively) with calving to first service. Strong genetic correlations existed between kilograms of ECM in early lactation and both delayed cyclicity (0.57 ± 0.14) and lnCLA (0.45 ± 0.09), whereas moderate genetic correlations (0.31 ± 0.18 and 0.25 ± 0.11) existed between kilograms of ECM in early lactation and lnIOI and lnILI, respectively. A strong

Table 3. Numbers of records (N), mean, and SD for the atypical progesterone profiles (per lactation) and for cycle length traits (all estrus cycles per lactation)

Trait ¹	N	Mean	SD	Median
Delayed cyclicity (0/1)	1,610	0.09	0.31	
Prolonged luteal phase (0/1)	1,610	0.13	0.36	
Cessation of cyclicity (0/1)	1,610	0.03	0.23	
C-LA (d)	1,592	31.9	17.5	27.9
ILI (d)	2,122	5.0	3.2	4.8
LPL (d)	3,376	18.7	10.4	16.7
IOI (d)	2,068	23.0	9.4	21.2

¹C-LA = commencement of luteal activity; ILI = interluteal interval; LPL = luteal phase length; IOI = interovulatory interval.

Table 4. Estimated heritability (h^2) and SE in parentheses, genetic (σ_A^2), permanent environment (σ_{pe}^2), and residual (σ_e^2) variances, and repeatability (t) for the traits analyzed

Trait	h^2	σ_A^2	σ_{pe}^2	σ_e^2	t
Delayed cyclicity	0.24 (0.05)	0.02	0.002	0.08	0.26
Prolonged luteal phase	0.02 (0.04)	0.002	0.003	0.12	0.04
Cessation of cyclicity	0.00 (0.04)	0.00	0.001	0.03	0.04
lnC-LA ¹	0.18 (0.04)	0.06	—	0.26	—
lnILI ¹	0.08 (0.14)	0.04	0.09	0.33	0.27
lnLPL ¹	0.08 (0.05)	0.02	0.01	0.19	0.13
lnIOI ¹	0.03 (0.04)	0.005	0.005	0.16	0.06

¹Natural log (ln) of C-LA = commencement of luteal activity; ILI = interluteal interval; LPL = luteal phase length; IOI = interovulatory interval.

negative genetic correlation (-0.60 ± 0.24) existed between delayed cyclicity and lnIOI. Because we detected no genetic variation for cessation of cyclicity, it was not included in the estimation of genetic correlations.

Luteal phase length in the last cycle was strongly negatively correlated with CFH and CInt (-0.72 ± 0.23 and -0.59 ± 0.45 , respectively). Interovulatory interval in the last estrus cycle before first AI was weakly genetically correlated with CFS (0.21 ± 0.08). Standard errors for all correlations between lnLPL and lnIOI with the traditional fertility measurements and ECM during the first 60 DIM were generally large, with some exceptions.

DISCUSSION

Exploitable genetic variation for delayed cyclicity and C-LA as well as strong genetic correlations with milk yield in early lactation implies possible deterioration in these traits if they are not considered in breeding goals. The existence of heritable genetic variation in these traits, coupled with the genetic correlations with traditional reproductive measures, suggests that such information can be useful to improve the genetic evaluation for fertility in HF cows.

Population Statistics

The prevalence of atypical P4 profiles in the present study (30.2%) was similar to an earlier study from Sweden (29.6%; Petersson et al., 2006a) but lower than reported for Holsteins in Belgium (49%; Opsomer et al., 2000) and France (46%; Cutullic et al., 2011). The definition of atypical profiles nonetheless differs between studies. Moreover, the present study included data from 4 countries differing in genetic ancestry, production systems, experimental treatments, as well as different sampling years. Furthermore, in the present study, the P4 profiles were edited and modeled using a computer algorithm. The prevalence of atypical P4 profiles was explained by a high incidence of prolonged luteal phases in all countries except the UK, which had a greater incidence of cessation of cyclicity. This is not in agreement with Petersson et al. (2006a), where a greater incidence of delayed cyclicity for Swedish cows was detected compared with the Swedish cows in the present study, and with Royal et al. (2000), who documented that prolonged luteal phase was the most common atypical P4 profile in UK HF cows (16.8%), whereas the incidence of prolonged luteal phases was only 6.4% in British Friesians.

Table 5. Genetic correlations (SE in parentheses) between the atypical progesterone (P4) profiles, cycle length traits, and traditional fertility measures and milk production¹

Item	Traditional fertility measure					
	CFH	CFS	PFS	IFLS	CInt	ECM
Delayed cyclicity	0.32 (0.26)	-0.14 (0.19)	1.00 (1.21)	0.32 (0.56)	NC ²	0.57 (0.14)
Prolonged luteal phase	-0.94 (1.11)	0.42 (0.56)	NC	0.30 (1.09)	NC	-0.60 (0.54)
lnC-LA ³	1.00 (0.17)	0.35 (0.12)	0.20 (0.43)	NC	0.54 (0.27)	0.45 (0.09)
lnILI ³	-0.17 (0.20)	-0.07 (0.15)	-0.36 (0.38)	NC	-0.03 (0.33)	0.25 (0.11)
lnLPL ³	-0.38 (0.19)	0.25 (0.14)	0.38 (0.18)	NC	0.03 (0.30)	-0.02 (0.10)
lnIOI ³	0.11 (0.29)	0.76 (0.24)	0.25 (0.42)	NC	NC	0.31 (0.18)

¹CFH = calving to first heat, CFS = calving to first service, PFS = pregnancy to first service, IFLS = interval from first to last service, CInt = calving interval, and ECM = kg of ECM during the first 60 DIM.

²NC = not converged.

³Natural log (ln) of C-LA = commencement of luteal activity; ILI = interluteal interval; LPL = luteal phase length; IOI = interovulatory interval.

The prevalence of normal and atypical P4 profiles differed between the 4 countries (Table 2). This may be attributed to several contributing factors, such as different management and production systems, as well as frequency of P4 testing. Sampling frequency is important because the accuracy of the derived profiles improves with greater frequency of testing. If samples are taken too infrequently, the risk of missing an important stage in the estrus cycle will increase. Because frequent milk sampling is difficult to manage on the commercial farm level, primarily because of the sampling costs, automated sampling and analysis of P4 (e.g., with Herd Navigator) is a future possibility.

Mean C-LA in the present study of 31.9 d (Sweden 30.6 d, the Netherlands 33.0 d, Ireland 34.1 d, and UK 27.3 d), was 1 to 4 d shorter than documented in some populations (Horan et al., 2005; Cutullic et al., 2011; Berry et al., 2012), but longer than reported by Darwash et al. (1997b) and Veerkamp et al. (2000), who documented mean C-LA of 28.7 and 29.5 d, respectively. Berry et al. (2012) used primiparous cows, whereas we included multiparous cows in the present study, which could have contributed to the difference in mean C-LA between studies. First-parity cows had longer C-LA than later-parity cows, which is in agreement with results by, for example, Petersson et al. (2006b).

The mean IOI of 22.8 d (SD = 10.5) for normal P4 profiles is similar to the 22.3 d (Royal et al., 2000), 22 d (Friggens and Labouriau, 2010), and 21.0 d (Horan et al., 2005) reported previously. Mean IOI for the first cycle in the present study of 23.9 d was slightly longer than in subsequent cycles, which is not in agreement with a previous Swedish study with Swedish Red and White cows (Ratnayake, 1996), where the first cycle was shorter than subsequent cycles. Nonetheless, the results reported by Royal et al. (2000) corroborate the present study, where HF cows had a longer first IOI (22.5 d) than British Friesian cows, and both studies had similar proportions of long, short, and normal IOI. Cows with delayed cyclicity profiles had the shortest IOI, with a mean of 20.2 d (SD = 8.6), whereas profiles with prolonged luteal phase and cessation of cyclicity had longer cycle lengths, which may lead to an increased time to service and thus interval to next calving.

We found a higher incidence of delayed cyclicity for cows calving in the spring and fall compared with summer-calving cows. Petersson et al. (2006a) documented a greater incidence of any atypical P4 profile in winter-calving cows, and Opsomer et al. (2000) reported a greater incidence of delayed cyclicity in winter-calving cows. Sweden, the Netherlands, and UK have intensive production systems, whereas Ireland has a more extensive pasture-based system and, according to Pollott and Coffey (2008), production system affects both ILI

and LPL. Petersson et al. (2006b) found that cows in tiestalls had a greater risk of atypical P4 profiles and that loose housing had a more favorable influence on ovarian activity in cows. Difference in production, management, and feeding systems as well as in temperature and light exposure may explain these seasonal differences in ovarian activity.

Genetic Parameters

To our knowledge, this is the first study to document genetic variation for atypical P4 profiles, with the exception of prolonged luteal phase in the first estrus cycle postpartum, for which Royal et al. (2002a) estimated the heritability to be 0.13 ± 0.06 in UK Holstein-Friesian cows. Significant genetic variation was detected in the present study for delayed cyclicity, which warrants further investigation to improve genetic evaluations for fertility in dairy cows. Because reproduction failure is one of the main reasons for culling (Ahlman et al., 2011), progesterone-based fertility measures provide an earlier and more objective physiological measure of reproduction performance. The earlier a producer can detect an atypical P4 profile, the easier it may be to detect cows with compromised fertility and to treat them accordingly, thereby possibly reducing calving interval and involuntary culling rates. Because test years and regions differed between the countries, genetic trends were not studied.

Delayed cyclicity and C-LA are physiologically very similar traits and had similar heritabilities (0.24 and 0.18, respectively). Because exploitable genetic variation exists for both traits, they could contribute usefully to a breeding program for improved fertility. The heritability for C-LA in the present study (0.18) was slightly greater than in earlier studies, where the heritability was estimated to be 0.13 (Berry et al., 2012) and 0.16 (Veerkamp et al., 2000; Royal et al., 2002a; Petersson et al., 2007). Low heritability was evident for prolonged luteal phase (0.02), ILI (0.08), and LPL (0.08). Very small genetic variation was detected for cessation of cyclicity. The standard errors of the heritability estimates for prolonged luteal phase, cessation of cyclicity, ILI, LPL, and IOI were large, however. The repeatability of most traits was low, except for delayed cyclicity (0.26), which was similar to that documented by Petersson et al. (2006b) in Swedish HF cows.

The antagonistic genetic correlations in the present study between milk production and traditional fertility traits agree with findings in different breeds (Berry et al., 2014). High milk production in early lactation was genetically correlated to delayed cyclicity, a longer C-LA, longer ILI, and longer IOI. A long C-LA was also genetically associated with longer CFH and

CFS intervals and to longer calving intervals, which is in agreement with results by Royal et al. (2002a) and Berry et al. (2012). Moreover, CFS was genetically associated with a longer LPL and IOI. To reduce IOI, CFH, and CFS, it is important that cows start cycling earlier after calving. Standard errors of the genetic correlations were large for most of the traits, albeit with some exceptions; we also observed a high incidence of nonconvergence in the bivariate analyses, which can probably be explained by the relatively small data set or by weak genetic links between the populations.

CONCLUSIONS

The genetic variation in delayed cyclicity and C-LA observed in the present study suggests that both traits could be useful indicators of fertility. Moreover, these measures were strongly genetically correlated with milk yield in early lactation, which may imply deterioration in these traits if not considered in breeding goals that also include selection for higher milk yield.

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