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Effect of Extending Voluntary Waiting Period on Health of Holstein Friesian Dairy Cows

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Abstract

The aim of this of this experimental study to investigate the effect of 3 voluntary waiting periods (VWP) on health of dairy cows. A total of 100 lactations of 100 Holstein Friesian cows with high milk production (average 9.442 ± 620 kg) were randomly (based on the ear tags digits of cows) distributed to 1 to 3 experimental groups with VWP of 50 (VWPG50; n = 32), 100 (VWPG100; n = 34) or 150 days (VWPG150; n = 34). Observations relating to diseases of the cows were made by the farm veterinarian and research personnel. Were defined eight disease: puerperal fever, retained fetal membranes, displaced abomasum, metritis, clinical ketosis, clinical mastitis, ovarian cysts, and claw diseases. The experimental days (ED) were from 4 days in milk (DIM) to 100 days after the next calving. The experiment was managed at Dairy Research Farm Şimnic-Craiova January 2018 to December 2022. A clear set of clinical signs were used to define a case at the diseases without the need for laboratory confirmation. Values of Lactational incidence risk (LIR) median postpartum days at diagnosis and pairwise comparison of proportion between VWPs were calculated. LIR for puerperal fiver, retained fetal membranes, displaced abomasum, clinical ketosis, clinical mastitis, ovarian cysts and claw disease were 4; 5; 2; 8; 8; and 4% respectively. Numerically, cows with VWP of 100 and150 days had more disease cases compared with VWP of 50 days. The differences between experimental groups of cows regarding proportions of cows with disease cases were not statistically significant. Any of the eight disorders reported in this study was analyzed independently to other health problems. For all enrolled cows (n = 100) VWP was extended until 100 or 150 days postpartum with no effect on the lactational incidence risk for the eight disorders analyzed.

Keywords

Voluntary Waiting Period, Dairy Cow Health, Lactation Disorders, Lactation Incidence Risk for Cow Diseases

1. Introduction

The Voluntary Waiting Period (VWP) is the interval after parturition in which the cows are not inseminated, even if they are seen in estrus. Traditionally, farmers were advised for one year calving interval (CI) for this cows, to realize one calf per cow per year, a yearly peak in milk yield, and to maximize milk income [1]. Around calving the cows face with multiple transitions, like drying off, calving itself, and the start of the start of the next lactation. All calving cows face these transitions every year.

The high-yielding cows in a one-year CI frequently have milk yields above 18 kg per day at the time of dry-off, which is a risk factor for intramammary infections in the dry off period and at calving [2] [3].

After parturition the uterus needs time to involute, and eliminate any placental residues or infection. Also, after calving the cows moves through the period of negative energy balance.

Purposely extending the lactation length by extending VWP for first insemination reduces the frequency of these challenging events.

Early lactation after calving is described as a moment of great importance for infection of the mammary glands. Also, during early lactation dairy cows experience a negative energy balance (NEB) because feed intake is inadequate to meet nutrient demands for milk production. Body reserves are mobilized which results in increased plasma non-esterified fatty acid (NEFA), β-hydroxybutyrate (BHBA), and liver triacylglycerol (TAG) concentrations. This metabolic changes are associated with impaired fertility. About two of reproductive disorders are encountered in the first month postpartum [4].

Recent changes in management of dairy herds may allow the length of the VWP to be modelated. Extending the length of the VWP may allow more time to recover the uterine health [5] [6] [7], for ameliorated immune status or more time to resolving the inflammatory processes after calving [8] [9]. A prolonged VWP may offer sufficient time to get back reproductive hormone secretion normal levels and a metabolic status that stimulates resumption of ovarian cyclicity [10] [11].

Postpartum uterine involution has many aspects that are interrelated (recovery of this uterus, degeneration of the myometrium, and regeneration of the endometrium) [12]. After parturition the uterus gradually restores to its normal size (pre-pregnancy size) by the contraction of the uterine muscles and the discharge of the uterine content [13]. The recovery time of the postpartum pregnant uterine horn is 25 days [12] and 30.1 ± 3.8 days in first calving cows and 30 ± 4.3 days in third—calving cows [14]. Zhang *et al.*, (2010) [15] indicated that diameter of the uterine horn tended to level off at day 25 postpartum in multiparous Chinese Holstein cows.

After fourth week, any damaged endometrial tissue regenerates, a wave of ovarian follicles develop, a dominant follicle is selected and estradiol secretion leads to ovulation and formation of a corpus luteum. The genital tract after six

weeks after calving should be capable of establishing the next pregnancy. But, about 50% of dairy cows have irregular ovarian cycles during the postpartum period and cows with abnormal vaginal discharge are more likely than normal cows to have delayed resumption of ovarian cycles after calving, or prolonged postpartum luteal phases [16]. Some research reports suggest how uterine diseases may disrupt endocrine signaling, oocyte, follicle and embryo development, and the uterine environment [17] [18] [19] [20] [21].

Extending the VWP is a strategy to reduce the frequency of calvings, and so to reduce the risk for diseases per unit of time [22]. Also an extended VWP could be connected with metabolic status and energy partitioning in dairy cows during different phases in lactation, if lactation is extended insemination of the cow takes place later in lactation (when milk yield is decreased). Also, insulin and insulin-like growth factor 1 (IGF-1) can be increased and reproductive performances can be ameliorated [23] [24]. Some authors reported that cows with extended lactation had more persistent lactation curves [25] [26], a lower milk production and increased body condition score (BCS) at the end of lactation [25] [26]. All of this aspects indicate a difference in energy partitioning between milk and body reserves in dairy cows. Some cows are more prone to partition energy toward milk production rather than toward body reserves [27] [25]. Marett *et al*., (2019) [28] reported that cows with a high milk production at 450 days in mil (18.9 kg/day) had a tendency for more lipid mobilization around 460 days in milk (DIM) and around 580 DIM compared with cows with 12.3 kg/day.

In spite of the possible benefits of extended VWP on reproductive performance, the consequence of this strategy on overall dairy herd performance has not been completely explicated. Extended lactations by extending VWP is a milk production system by which cows are handling for increased milk persistency and rebreeding at 18 months instead of 12 months [29]. Currently the average productive life time is around 3.0 lactations. In each lactation there is an accumulation of health disorders in the period between parturition and peak lactation. Using a 2 x 18 months lactation cycles, the health disorders would decrease by one-third. Also, the reduction of number of lactation cycles may reduce the number of surplus calves and labor at drying off, parturition and disorder treatments.

Extending lactations by extending VWP would increase calving [29] [30]. Calving interval (CI) was the classic parameter for monitoring the status of productive, reproductive or health programs in dairy cows. One year CI was recommended, but in reality CI surpass 1 year [1].

The overall impact of extended lactation on milk production would therefore be best expressed as milk yield per day of calving interval (MY/CI) [27].

For the longer CI MY/CI will only increase with extended lactations if milk yield level relative to peak yield is adequately maintained, and this is more frequently in case for moderate compared with extreme extensions of the VWP, and more for primiparous cows compared with multiparous cows [25] [26].

Limited reports were published regarding disease incidence of dairy cows with

extended lactations. Burgers *et al*., 2022, [31] reported no effect of VWP on disease treatments but per year the number of disease treatments were lower for extended VWP to 125 and 200 days.

There are a range of diseases affecting dairy cows with different impact on health and welfare.

The suboptimal health of dairy cows after parturition, negative energy balance and immune suppression occur concurrently leaving cows receptive to infections and metabolic disorders [32].

Deliberately extending the lactation duration by extending the VWP, reduces the frequency of challenging events [1].

The aim of this experimental study was to investigate the effects of 3 VWPs (50, 100 and 150 days) on health of Holstein Friesian dairy cows.

2. Materials and methods

Animals and management

Dairy cows enrolled in this experiment were located at Agricultural Research and Development Station (ARDS) Şimnic-Craiova, SW Romania (182 m above sea level, 44˚19'N, 23˚48'E).

The experiment was performed in compliance with European Union Directive 86/609/Ec. and National legislation on Holstein Friesian dairy cows with high-milk-production. The experiment was managed at Dairy Research farm (Şimnic-Craiova) between January 2018 and December 2022. All cows were chosen using the following criteria: good general health status, no twin pregnancy, no clinical mastitis or SCC > 250000 of the final 2 milk test days prior to dry-off. The experimental days (ED) were from 40 DIM after calving to 100 days after the next calving.

The culled cows were observed until the cows were culled. Nutritional and management strategies for dairy cows were used to prepare the animals for lactation and to minimize the incidence of disease disorders after calving.

Pregnant cows are dried-off 50 ± 10 days before the expected calving date, and are moved in a dry-pens (for multiparous) after last milking, and pregnant heifers are moved in a separate pens (for heifers). All pregnant animals are grouped as far-off dry (from 50 to 22 days prior expected calving date), close-up dry (from 21 to 0 days prior expected calving date), and fresh (from 0 to 21 days after calving date). For the far-off period multiparous cows are fed a low energy diet (14% starch and 46% forage NDF) or a higher energy diet (>14% starch if cows are in poor condition, BCS less than 2.5). For the close-up period multiparous cows are fed a higher – forage NDF (≥46% forage NDF), and for the fresh period multiparous cows are fed higher–starch diet (27% starch). Similar to multiparous cows the pregnant heifers are fed a low energy for-off diet, higher-forage NDF close-up and higher-starch fresh diet. Optimal Dietary Cation Anion Difference (DCAD) o prepartum diets is –5 mEq/100 g of feed Dry Mater (DM) and lactating diets is 27 mEq/100 g of feed DM.

The aim of nutritional strategies is to minimize the excessive prevalence of elevated βeta-Hydroxybutyrate concentrations, maximize reproductive performance, and to reduce disorder incidence in early postpartum period.

Forage, a small amount of concentrate and a trace of mineral salts constituted the dry cows ration using early dry-off period.

Subsequently a close up ration was fed which provides additional nutrients. At 3 weeks before expected calving date the cows were moved into the close-up pen, where farm workers or research personnel monitor the calving process and postpartum (PP) events.

After calving the feed rations were calculated to provide recommended nutrients for lactating cows. All necessary feeds consisting of corn silage, haylage, chopped green alfalfa, fodder beet and grains are produced locally. The concentrate feeding levels increased gradual at 1 kg/day at calving to 9-10 kg/day from 21 DIM to 100 DIM of each cow. After 100 DIM concentrate feeding levels decreased to suit diminution in milk production (on last 7 days calculations). Additionally, all cows have access to pasture (alfalfa or ryegrass). The lactating cows were milked two times a day (05:00 a.m. and 17:00 p.m.) in a classic DeLaval milking system and were housed free in barns bedded with straw. Cows have ad libitum access to fresh water.

Experimental design

For this experiment a total of 100 cows were enrolled (30 primiparous and 70 multiparous cows) and were randomly (based on the tags digits of cows) distributed to 1 of the 3 experimental groups with a voluntary waiting period (VWP) of 50 (VWPG50; n = 32), 100 (VWPG100; n = 34) or 150 days (VWPG150; n = 34).

We eliminated all cows with twin pregnancy because twin pregnancies are the main non-infectious factors compromising pregnancy maintenance within the first 90 days of gestation [33] [34] [35]. Also cows with clinical mastitis or Somatic cell count (SCC) > 250.0000 prior to dry off were eliminated because this cows are more prone to ketosis or other periparturient diseases as metritis, retained placenta or lameness after parturition [36].

Observation relating to diseases of the cows post calving were made by the farm veterinarian and research personnel. Cows were observed for: retained fetal membranes (RFM); metritis; ovarian cysts (OC), clinical mastitis; claw disease (CD); milk fever (MF); ketosis; and displaced abomasum (DA). For all eight disorders, a clear set of clinical signs were used to define a case of the disease. The RFM was characterized by presence of fetal membranes more than 12 hour after calving.

Metritis was characterized by enlarged uterus with fetid watery red-brown vaginal discharge and with a rectal temperature ≥ 39.5°C.

Ovarian cysts are characterized as structures greater than 2.5 cm in diameter remaining on an ovary for more than 10 days. Major category of cysts include follicular cysts, luteinized follicular cysts and cystic corpora luteal.

Clinical mastitis was characterized by the presence by the presence of abnor-

mal milk or by signs of inflammation in 1 or more quarters.

Cows walked with arched back and had short strides in 1 or more legs were characterized with claw disease (laminitis = disorder of the corium of claws).

Milk fever or hypocalcemia is a calcium deficiency. The clinical signs of MF are divided into three stages: in stage 1 cows are mobile but show signs of hypersensitivity and excitability such as restlessness, tremor, ear twitching, heat bobbing and mild ataxia. If not treated, symptoms progress to stage 2: cow present sternal recumbency, tachycardia, and smoot muscle paralysis, and cows often tuck their heads into their flanks. In stage 3 cows present lateral recumbency, muscle flaccidity, unresponsiveness to stimuli and loss of consciousness progressing to coma. Ketosis is an elevated concentration of ketone bodies (acetone, acetoacetate and beta hydroxybutyrate—BHB) in all body fluids. Dipstick tests that measure acetoacetate and acetone concentrations in urine are reasonably accurate when interpreted within 5-10 seconds. Milk dipstick tests that measure BHB concentration are also reasonably accurate and take 1-2 minutes to react.

These dipsticks are read by observation of a particular color change and are semi quantitative. For this experiment we used a dipstick containing the salt nitroprusside which becomes pink in the presence of acetoacetate. Tests were performed as described aby the manufacturer on urination induced by manual stimulation of the area below the vulva. The results are expressed in five categories: (1) negative (0 mg/dl); (2) trace (5 mg/dl); (3) small (15 mg/dl); (4) moderate (40 mg/dl); (5) large (greater than 80 mg/dl) of acetoacetate.

Using the categories 2 [trace (5 mg/dl)]; 3 [small (15 mg/dl)]; 4 [moderate (40 mg/dl)] and 5 [large (greater than 80 mg/dl)] to diagnose subclinical ketosis and clinical ketosis have good sensitivity (88%) and specificity (95%) [37].

Clinical signs for displaced abomasum (DA) (Left DA and Right DA) and abomasal volvulus include anorexia and decreased milk production.

The most important diagnostic finding is a ping upon simultaneous percussion and auscultation of the abdomen, in the area marked by a line from the tuber coxae to the point of elbow, and from the elbow toward the stifle on both sides of the cow. The ping associated with LDA is most commonly located in an area between ribs 9 and 13 in the middle to upper third of the left abdomen and for RDA is most commonly in the area between ribs 10 and 13 on the right abdomen.

Statistical analysis

All data were entered into Microsoft Excel Computer Program 2007 and were statistically evaluated. Value as lactational incidence risk (LIR), and median postpartum days at diagnosis were calculated for all, primiparous and multiparous cows and for experimental groups (VWPG50; VWPG100, and VWPG150).

All P-values of pair vise comparations of the 3 experimental VWPs also were calculated.

Odds ratio were calculated using MedCalc Software Ltd (version 22.023) [38].

3. Results

A total of 41% of cows (primiparous + multiparous cows) had postpartum disorders and the lactational incidence risk of puerperal fever, retained fetal membranes, displaced abomasum, metritis, clinical ketosis, clinical mastitis, ovarian cysts and claw disease were: 4; 5; 2; 8; 2; 8; 8; and 4% respectively (Table 1).

Some diseases such as clinical ketosis and claw disease were not diagnosed in VWP Group 50 and in VWP Group 100 cows respectively (Table 2).

Table 1. Lactational incidence risks (LIR) and median days in milk for the eight disorders after calving.

Disorder[2]	LIR, all		LIR primiparous		LIR multiparous		Median DIM at diagnosis
	n	%	n	%	n	%	
1. Puerperal fever	4	4	1	3.3	3	4.3	1
2. Retained fetal membranes	5	5	1	3.3	4	5.7	1
3. Displaced abomasum	2	2	-	-	2	2.8	20
4. Metritis	8	8	3	10	5	7.1	24
5. Clinical ketosis	2	2	1	3.3	1	1.4	28
6. Clinical mastitis	8	8	3	10	5	7.1	52
7. Ovarian cysts	8	8	2	6.7	6	8.7	60
8. Claw diseases	4	4	-	-	4	5.7	78
Total	1	41	11	36.6	30	42.8	33

Table 2. Disease numbers for the 3 experimental groups with a voluntary waiting period of 50, 100 and 150 days.

	VWPG50		VWPG100		VWPG150		Total	
	n	%	n	%	n	%	n	%
Number of cows	32	32	34	34	34	34	100	100
Puerperal fever	1	3.1	2	5.9	1	2.9	4	4
Retained fetal membranes	1	3.1	2	5.9	2	5.9	5	5
Displaced abomasum	1	3.1	1	2.9	-	-	2	2
Metritis	2	6.2	3	8.8	3	8.8	8	8
Clinical ketosis	-	-	1	2.9	1	3	2	2
Mastitis	3	9.4	2	5.9	3	8.8	8	8
Ovarian cysts	2	6.2	3	8.8	3	8.8	8	8
Claw disease	1	3.1	-	-	3	8.8	4	4
Total number of cases (%)	11	34.4	14	41.1	16	47	41	41

Table 3. Comparison of proportions (expressed as percentage) of total number of cases between the experimental groups of cows with a VWP of 50, 100 and 150 days, an odds ratios for associations among VWP Groups.

	VWPG*50 versus VWPG100	VWPG50 vs. VWPG150	VWPG100 vs. VWPG150
1. Difference %	6.7	12.6	5.9
95% confidence interval	−16 to 28.4	−10.7 to 33.9	−16.8 to 27.8

Continued

Chi-squared	0.310	1.066	0.237
Degree of freedom	1	1	1
Significance level	P = 0.5578	P = 0.3018	P = 0.6267
2. Odds ratio	1.3364	1.6970	1.2698
95% confidence interval	0.492 to 3.630	0.629 to 4.580	0.486 to 3.314
Significance level	P = 0.5696	P = 0.2965	P = 0.6254

*VWPG = voluntary waiting period group.

We found lower LIR values of displaced abomasum, and clinical ketosis probably as a result of good health service and production management. Fleischer *et al.*, 2001, [39] reported LIR values for displaced abomasum and clinical ketosis of 1.1% and 1.7% respectively.

Higher LIR values in this study were found for metritis, mastitis and ovarian cysts (Table 1). Intermediate LIR values were found for puerperal fever, claw disease and retained fetal membranes (Table 1).

Numerically, cows with extended VWP of 100 and 150 days had more disease cases compared with cows with extended VWP of 50 days (14 and 16 cases versus 11 cases).

Comparison of proportions, expressed as percentage of disease cases from each experimental group revealed that differences were not statistically significant.

Also odds ratio were calculated to see if odds in extended VWPG 100 or extended VWPG 150 are significantly higher than VWPG 50.

P-values were > 0.05 and we concluded that the odds ratio was not significantly different from1 and that the odds in VWPG 100 and in VWPG 150 were not higher than in VWPG 50 (Table 3).

4. Discussion

The lactational incidence risk of diseases in dairy cows and their detrimental effects are accepted [40] [41]. Reproductive disorders (RFM, Metritis and Ovarian cysts) were found in 21% of all 100 cows enrolled in this, and a higher incidence was in multiparous cows (15%), compared with primiparous cows (6%) (Table 1).

Metabolic disorders (puerperal fever, DA, clinical ketosis, and claw disease). Were found in 12% of all 100 cows and a higher incidence was in multiparous cow (14.2%) compared with primiparous cows (6.6%) (Table 1). Mastitis was found in 8% of all 100 cows enrolled in this study (Table 1); 10% in primiparous cows and 7.1 in multiparous cows.

The overall incidence of reproductive disorders found in this study 21% was in accordance with the result (21.6%) reported by Carvalho *et al.*, (2019) [42]. Also they reported higher values for mastitis 15.3% and for lameness 10.5% compared with our results of 8% for mastitis and of 4% for lameness.

Metabolic problems derive from difficulties cows have to adapt to large variations and disturbances occurring outside and inside the organism. Carvalho *et*

al., (2019) [43] showed that consequences of postpartum clinical disease are not limited to the period of clinical illness but are extended to period after the clinical resolution of the disease, and the long term consequences of disease are more difficult to be measured.

Increasing VWP until 100 days affected the number of disorder cases (11 cases vs. 14 cases) but the difference between proportions expressed as percentage was not statistically significant.

When extending VWP further, until 150 days, numerically disorder cases increased from 14 to 16 cases, but the differences were not statistically significant. Also odds ratios in extended VWPG 100 or VWPG 150 were not significantly higher than VWPG 50.

Infection diseases such as metritis and mastitis are a common polymicrobial diseases after parturition and cumulative incidence ranges from 10% to 25% and from 5% to 75% respectively, of cows in the lactation period. In this study we found 8% metritis cases and 8% mastitis cases, and median DIM at diagnosis was 28 and 52 respectively.

There is evidence that the high-grain diets after calving are associated with the release of high amounts of endotoxin in rumen fluid [36]. If infected, the mammary gland and uterus additionally are important source of endotoxin. The endotoxin translocated from rumen, uterus or mammary gland into the systemic blood circulation trigger chronic low-grade inflammatory conditions associated with multiple disease (mastitis, RFM, metritis, laminitis, DA, milk fever, fatty liver, and downer cow syndrome). Endotoxin include membrane components deriving from Gram-negative and Gram-positive bacteria including Lipopolysaccharide (LPS) and Lipoteichoic Acid (LTA). Data reported by Eckel an Ametaj (2020) [36] showed that cows treated with a combination of LPS and ATA both orally and subcutaneously had 60% lower clinical cases of mastitis, 12% lower clinical cases of endometritis, 8% lower cases of udder edema, 33% lower number of dead cows, and the number of healthy cows in the treatment group was 150% higher than the control group of cows.

Some of the disorders occurring in the early lactation such as Puerperal fever or Retained Fetal membranes, increase the risk of diseases later during the current and following lactation. Fleischer *et al*., 2001, [39] reported that dairy cows suffering from puerperal fever were at 1.4 (1.1 - 1.7) and 1.7 (1.3 - 2.2) significantly ($P \leq 0.05$) greater risk of suffering from metritis and clinical mastitis, respectively in the current lactation. Also, Retained Fetal Membranes was significantly ($P \leq 0.05$) associated with 3.0 (2.6 - 3.5) times higher lactational incidence risk of metritis, which was a significant ($P \leq 0.05$) risk factor for ovarian cysts. These associations support the idea that health problems in dairy cows tend to occur as a complex (health disorder complexes) and this means that once a disorder was diagnosed, the farmer or the veterinarian would observe the cow more closely for other diseases [43]. We did not analyze some of this associations within the framework of our study because more data is necessary.

5. Conclusions

For all enrolled cows (n = 100); VWP was extended until 100 or 150 days postpartum with no effect on the lactational incidence risk for eight disorders analyzed.

Any of the eight disorders reported in this study was analyzed independently of other health problems.

A customized strategy based on individual cow characteristics is a future approach to select suitable cows for an extended lactation by extending VWP in modern dairy farming.

Data from this experiment highlight the importance of considering lactational incidence risks for postpartum disease when defining VWP duration for lactating dairy cows.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] van Knegsel, A.T.M., Burgers, E.E.A., Ma, J., Goselink, R.M.A. and Kok, A. (2022) Extending Lactation Length: Consequences for Cow, Calf, and Farmer. *Journal of Animal Science*, **100**, skac220. https://doi.org/10.1093/jas/skac220

[2] Odensten, M.O., Berglund, B., Waller, K.P. and Holtenius, K. (2007) Metabolism and Udder Health at Dry-Off Cows of Different Breeds and Production Levels. *Journal of Dairy Science*, **90**, 1417-1428.

[3] Nitz, J., Wente, N., Zhang, Y., Klocke, D., tho Seeth, M. and Krömker, V. (2021) Dry Period or Early Lactation—Time of Onset and Associated Risk Factors for Intramammary Infections in Dairy Cows. *Pathogens*, **10**, Article No. 224. https://doi.org/10.3390/pathogens10020224

[4] Sammad, A., Khan, M.Z., Abbas, Z., Hu, L., Ullah, Q., Wang, Y., Zhu, H. and Wang, Y. (2022) Major Nutritional Metabolic Alterations Influencing the Reproductive System of Post-Partum Dairy Cows. *Metabolites*, **12**, Article No. 60.

[5] Gilbert, R.O., Shin, S.T., Guard, C.L., Erb, H.N. and Frajblat, M. (2005) Prevalence of Endometritis and Its Effects on Reproductive Performance of Dairy Cows. *Theriogenology*, **64**, 1879-1888.

[6] Gautam, G., Nakao, T., Yusuf, M. and Koike, K. (2009) Prevalence of Endometritis during the Postpartum Period and Its Impact on Subsequent Reproductive Performance in Two Japanese Dairy Herds. *Animal Reproduction Science*, **116**, 175-187. https://doi.org/10.1016/j.anireprosci.2009.02.001

[7] Sheldon, I.M., Cronin, J., Goetze, L., Donofrio, G. and Schuberth, H. (2009) Defining Postpartum Uterine Disease and the Mechanisms of Infection and Immunity in the Female Reproductive Tract in Cattle1. *Biology of Reproduction*, **81**, 1025-1032. https://doi.org/10.1095/biolreprod.109.077370

[8] LeBlanc, S.J., Osawa, T. and Dubuc, J. (2011) Reproductive Tract Defense and Disease in Postpartum Dairy Cows. *Theriogenology*, **76**, 1610-1618. https://doi.org/10.1016/j.theriogenology.2011.07.017

[9] LeBlanc, S.J. (2014) Reproductive Tract Inflammatory Disease in Postpartum Dairy

Cows. *Animal*, **8**, 54-63.

[10] Kawashima, C., Matsui, M., Shimizu, T. and Miyamoto, A. (2012) Nutritional Factors That Regulate Ovulation of the Dominant Follicle during the First Follicular Wave Postpartum in High-Producing Dairy Cows. *The Journal of Reproduction and Development*, **58**, 10-16.

[11] Cheong, S.H., Filho, O.G.S., Absalón-Medina, V.A., Pelton, S.H., Butler, W.R. and Gilbert, R.O. (2016) Metabolic and Endocrine Differences between Dairy Cows That Do or Do Not Ovulate First Postpartum Dominant Follicles. *Biology of Reproduction*, **94**, Article No. 18.

[12] Dai, T., Ma, Z., Guo, X., Wei, S., Ding, B., Ma, Y., *et al.* (2023) Study on the Pattern of Postpartum Uterine Involution in Dairy Cows. *Animals*, **13**, Article No. 3693. https://doi.org/10.3390/ani13233693

[13] Heppelmann, M., Krach, K., Krueger, L., Benz, P., Herzog, K., Piechotta, M., *et al.* (2015) The Effect of Metritis and Subclinical Hypocalcemia on Uterine Involution in Dairy Cows Evaluated by Sonomicrometry. *Journal of Reproduction and Development*, **61**, 565-569. https://doi.org/10.1262/jrd.2015-015

[14] Miettinen, P.V.A. (1989) Uterine Involution in Finnish Dairy Cows. *Acta Veterinaria Scandinavica*, **31**, 181-185. https://doi.org/10.1186/bf03547560

[15] Zhang, J., Deng, L.X., Zhang, H.L., Hua, G.H., Han, L., Zhu, Y., *et al.* (2010) Effects of Parity on Uterine Involution and Resumption of Ovarian Activities in Postpartum Chinese Holstein Dairy Cows. *Journal of Dairy Science*, **93**, 1979-1986. https://doi.org/10.3168/jds.2009-2626

[16] Opsomer, G., Gröhn, Y.T., Hertl, J., Coryn, M., Deluyker, H. and de Kruif, A. (2000) Risk Factors for Post Partum Ovarian Dysfunction in High Producing Dairy Cows in Belgium: A Field Study. *Theriogenology*, **53**, 841-857. https://doi.org/10.1016/s0093-691x(00)00234-x

[17] Bromfield, J.J., Santos, J.E.P., Block, J., Williams, R.S. and Sheldon, I.M. (2015) Physiology and Endocrinology Symposium: Uterine Infection: Linking Infection and Innate Immunity with Infertility in the High-Producing Dairy Cow. *Journal of Animal Science*, **93**, 2021-2033. https://doi.org/10.2527/jas.2014-8496

[18] Horlock, A.D., Piersanti, R.L., Ramirez-Hernandez, R., Yu, F., Ma, Z., Jeong, K.C., *et al.* (2020) Uterine Infection Alters the Transcriptome of the Bovine Reproductive Tract Three Months Later. *Reproduction*, **160**, 93-107.

[19] Moore, S.G., Ericsson, A.C., Behura, S.K., Lamberson, W.R., Evans, T.J., McCabe, M.S., Poock, S.E. and Lucy, M.C. (2019) Concurrent and Long-Term Associations between the Endometrial Microbiota and Endometrial Transcriptome in Postpartum Dairy Cows. *BMC Genomics*, **20**, Article No. 405.

[20] Piersanti, R.L., Horlock, A.D., Block, J., Santos, J.E.P., Sheldon, I.M. and Bromfield, J.J. (2019) Persistent Effects on Bovine Granulosa Cell Transcriptome after Resolution of Uterine Disease. *Reproduction*, **158**, 35-46.

[21] Ribeiro, E.S. (2018) Symposium Review: Lipids as Regulators of Conceptus Development: Implications for Metabolic Regulation of Reproduction in Dairy Cattle. *Journal of Dairy Science*, **101**, 3630-3641.

[22] Friggens, N.C., Andersen, J.B., Larsen, T., Aaes, O. and Dewhurst, R.J. (2004) Priming the Dairy Cow for Lactation: A Review of Dry Cow Feeding Strategies. *Animal Research*, **53**, 453-473.

[23] Wathes, D.C., Bourne, N., Cheng, Z., Mann, G.E., Taylor, V.J. and Coffey, M.P. (2007) Multiple Correlation Analyses of Metabolic and Endocrine Profiles with Fer-

tility in Primiparous and Multiparous Cows. *Journal of Dairy Science*, **90**, 1310-1325.

[24] Niozas, G., Tsousis, G., Steinhöfel, I., Brozos, C., Römer, A., Wiedemann, S., *et al.* (2019) Extended Lactation in High-Yielding Dairy Cows. I. Effects on Reproductive Measurements. *Journal of Dairy Science*, **102**, 799-810. https://doi.org/10.3168/jds.2018-15115

[25] Niozas, G., Tsousis, G., Malesios, C., Steinhöfel, I., Boscos, C., Bollwein, H. and Kaske, M. (2019) Extended Lactation in High-Yielding Dairy Cows. II. Effects on Milk Production, Udder Health and Body Measurements. *Journal of Dairy Science*, **102**, 811-823.

[26] Burgers, E.E.A., Kok, A., Goselink, R.M.A., Hogeveen, H., Kemp, B. and van Knegsel, A.T.M. (2021) Effects of Extended Voluntary Waiting Period from Calving until First Insemination on Body Condition, Milk Yield, and Lactation Persistency. *Journal of Dairy Science*, **104**, 8009-8022.

[27] Lehmann, J.O., Fadel, J.G., Mogensen, L., Kristensen, T., Gaillard, C. and Kebreab, E. (2016) Effect of Calving Interval and Parity on Milk Yield per Feeding Day in Danish Commercial Dairy Herds. *Journal of Dairy Science*, **99**, 621-633. https://doi.org/10.3168/jds.2015-9583

[28] Marett L.C., Auldist, M.J., Wales, W.J., Macmillan, K.L., Dunshea, F.R. and Leury, B.J. (2019) Responses to Metabolic Challenges in Dairy Cows with High or Low Milk Yield during an Ex-Tended Lactation. *Journal of Dairy Science*, **102**, 4590-4605.

[29] Knight, C.H. (2005) Extended Lactation: Turning Theory into Reality. *Advances in Dairy Technology*, **17**, 113. https://wcds.ualberta.ca/wp-content/uploads/sites/57/wcds_archive/Archive/2005/Manuscripts/Knight.pdf

[30] Sehested, J., Gaillard, C., Lehmann, J.O., Maciel, G.M., Vestergaard, M., Weisbjerg, M.R., *et al.* (2019) Review: Extended Lactation in Dairy Cattle. *Animal*, **13**, s65-s74. https://doi.org/10.1017/s1751731119000806

[31] Burgers, E.E.A., Kok, A., Goselink, R.M.A., Hogeveen, H., Kemp, B. and van Knegsel, A.T.M. (2022) Revenues and Costs of Dairy Cows with Different Voluntary Waiting Period Based on Data of a Randomized Control Trial. *Journal of Dairy Science*, **105**, 4171-4188.

[32] Esposito, G., Irons, P.C., Webb, E.C. and Chapwanya, A. (2014) Interactions between Negative Energy Balance, Metabolic Diseases, Uterine Health and Immune Response in Transition Dairy Cows. *Animal Reproduction Science*, **144**, 60-71.

[33] López-Gatius, F. and García-Ispierto, I. (2010) Ultrasound and Endocrine Findings That Help to Assess the Risk of Late Embryo/Early Foetal Loss by Non-Infectious Cause in Dairy Cattle. *Reproduction in Domestic Animals*, **45**, 15-24. https://doi.org/10.1111/j.1439-0531.2010.01620.x

[34] Mur-Novales, R., Lopez-Gatius, F., Fricke, P.M. and Cabrera, V.E. (2018) An Economic Evaluation of Management Strategies to Mitigate the Negative Effect of Twinning in Dairy Herds. *Journal of Dairy Science*, **101**, 8335-8349. https://doi.org/10.3168/jds.2018-14400

[35] López-Gatius, F., Garcia-Ispierto, I. and Hunter, R.H.F. (2020) Twin Pregnancies in Dairy Cattle: Observations in a Large Herd of Holstein-Friesian Dairy Cows. *Animals*, **10**, Article No. 2165. https://doi.org/10.3390/ani10112165

[36] Eckel, E.F. and Ametaj, B.N. (2016) Invited Review: Role of Bacterial Endotoxins in the Etiopathogenesis of Periparturient Diseases of Transition Dairy Cows. *Journal*

of Dairy Science, **99**, 5967-5990.

[37] Galvão, K.N., Neto, A.V., Peña, G., Bittar, J. and Ibarbia, L. (2012) Comparing the Urine Ketone Strip Test and the Handheld Ketone Meter to Diagnose Ketosis in Early Lactation Dairy Cows: VM186/VM186, 10/2012. Data Information Source Publication VM 186. University of Florida/IFAS Extension, 1-4.

[38] https://www.medcalc.org/calc/odds_ratio.php

[39] Fleischer, P., Metzner, M., Hoedemaker, M., Šlosárková, S. and Skřivánek, M. (2001) Clinical Disorders in Holstein Cows: Incidence and Associations among Lactational Risks Factors. *Acta Veterinaria Brno*, **70**, 157-165. https://doi.org/10.2754/avb200170020157

[40] Gilbert, R.O. (2016) Management of Reproductive Disease in Dairy Cows. *Veterinary Clinics of North America*: *Food Animal Practice*, **32**, 387-410.

[41] Fukushima, Y., Kino, E., Furutani, A., Minamino, T., Mikurino, Y., Horii, Y., *et al.* (2020) Epidemiological Study to Investigate the Incidence and Prevalence of Clinical Mastitis, Peracute Mastitis, Metabolic Disorders and Peripartum Disorders, on a Dairy Farm in a Temperate Zone in Japan. *BMC Veterinary Research*, **16**, Article No. 389. https://doi.org/10.1186/s12917-020-02613-y

[42] Carvalho, M.R., Peñagaricano, F., Santos, J.E.P., DeVries, T.J., McBride, B.W. and Ribeiro, E.S. (2019) Long-Term Effects of Postpartum Clinical Disease on Milk Production, Reproduction, and Culling of Dairy Cows. *Journal of Dairy Science*, **102**, 11701-11717.

[43] Gröhn, Y.T., Erb, H.N., McCulloch, C.E. and Saloniemi, H.S. (1989) Epidemiology of Metabolic Disorders in Dairy Cattle: Association among Host Characteristics, Disease, and Production. *Journal of Dairy Science*, **72**, 1876-1885.