Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria (INIA)
Available online at www.inia.es/sjar
http://dx.doi.org/10.5424/sjar/2013113-4140

Spanish Journal of Agricultural Research 2013 11(3): 718-735
ISSN: 1695-971-X
eISSN: 2171-9292

Effects of main reproductive and health problems on the performance of dairy cows: a review

N. Ghavi Hossein-Zadeh

Department of Animal Science. Faculty of Agricultural Sciences. University of Guilan. P.O. Box 41635-1314. Rasht, Iran

Abstract

This review focuses on the potential effects of twinning, dystocia, stillbirth, abortion, retained placenta and metritis on the productive and reproductive performances in dairy cattle. These are diverse disorders that are similar in that they all can result in impaired performance of dairy cows. Reproductive problems occur frequently in lactating dairy cows and can dramatically affect reproductive efficiency in a dairy herd. Poor reproductive performance is a major cause of involuntary culling and therefore reduces the opportunity for voluntary culling and has a negative influence on the subsequent productivity of a dairy herd. Reproductive performance is influenced by the interactive effect of environment, management, health, and genetic factors. In addition, diseases mainly affect dairy cow productivity by decreasing reproductive efficiency, shortening the expected length of productive life and by lowering milk production. Deciding whether to breed, treat, or cull dairy cows showing one or more of these problems is a challenge for both veterinarians and dairy producers. In addition, there is considerable debate among dairy scientists and bovine practitioners regarding the economic impact of these problems in a dairy operation and the most effective management or therapeutic intervention for treating them. Because of this controversy, dairy managers should focus on prevention and control of risk factors associated with each problem rather than on prescriptive therapeutic interventions.

Additional key words: dairy cow; diseases; reproductive disorders; productive performance; reproductive performance.

Introduction

Reproductive efficiency is a critical component of a successful dairy operation and acts as an important component of a profitable dairy farm, whereas reproductive inefficiency is one of the most costly problems facing the dairy industry today. Reproductive problems occur frequently in lactating dairy cows and can dramatically affect reproductive efficiency in a dairy herd. Some of the most common problems include twinning, dystocia, abortion, stillbirth, retained placenta and metritis. These are diverse disorders that are similar in that they all can result in impaired reproductive function. Deciding whether to breed, treat, or cull dairy cows exhibiting one or more of these reproductive problems is a challenge for both veterinarians and dairy producers. In addition, there is considerable controversy among dairy scientists and bovine practitioners regarding the economic impact of these problems in a dairy operation and the most effective management or therapeutic intervention for treating them. Because of this controversy, dairy managers should focus on prevention and control of risk factors associated with each problem rather than on prescriptive therapeutic interventions. Dairy producers should work closely with their herd veterinarian to develop such management strategies and discuss appropriate interventions when necessary (Fricke, 2001).

Low fertility reduces the profit by decreasing the average milk production and the number of calves per cow per year. Poor reproductive performance is a major cause of involuntary culling and therefore reduces the

* Corresponding author: nhosseinzadeh@guilan.ac.ir; navid.hosseinzadeh@gmail.com
Received: 28-02-13. Accepted: 12-07-13.

Abbreviations used: ACTH (adrenocorticotropin hormone); BCS (body condition score); CVM (complex vertebral malformation); DIM (days in milk); DMI (dry matter intake); FPI (foeto-pelvic incompatibility); FSH (follicle-stimulating hormone); HDL (high density lipoprotein); MET (metritis); NEB (negative energy balance); RP (retained placenta); UMPS (uridine monophosphate synthase).

opportunity for voluntary culling and has a negative effect on the future productivity of a dairy herd. Reproductive performance is influenced by the interactive effect of environment, management, health, and genetic factors (Gröhn & Rajala-Schultz, 2000; Roxström *et al.*, 2001).

Parturition is intimately interlocked with lactogenesis in all mammals. In dairy cows, it marks the start of the lactation and therefore the beginning of the productive cycle and is essential to the long-term sustainability of the farm. However, it is also a high-risk time for both mother and offspring leading to high veterinary and labor costs for the dairy cattle industry when complications occur. While complex physiological changes are occurring in the mother, the offspring has to make the transition from fetal life to extra-uterine life which can prove to be challenging. Parturition in cattle is a complex process that is triggered by the fetus and managed by a cascade of hormonal actions and physiological changes (Senger, 2003). Therefore, it seems logical that when complications occur, this has potential effect on normal bodily functions. It also provides newborn heifers that will become future lactating animals. Calvings are therefore sources of short and long-term income to producers.

The transition period is generally recognized as the most critical period of the lactation cycle for a dairy cow. The endocrine and physiological changes that accompany parturition and the onset of milk production negatively affect immune function and dry matter intake (DMI). As a result of nutrient demand for milk production increasing faster than DMI, cows experience a period of negative energy balance of varying duration and intensity. Early lactation is also a critical time for metabolic disorders, of which most occur during the first 2 wk postpartum (Goff & Horst, 1997). The extent of negative energy balance is related to the incidence and severity of most metabolic disorders, such as ketosis, displaced abomasum, retained placenta, and susceptibility to infections (Grummer *et al.*, 2004). In addition, improved energy balance has been proven to result in greater reproductive efficiency through earlier resumption of ovulatory cycles (Butler, 2005). Early resumption of cycles is important because conception rates increase with successive cycles (reviewed by Butler, 2003). Enhancing nutrient intake seems, therefore, imperative to maximize health and reproduction of periparturient cows.

This review addresses the possible consequences of some reproductive and health problems (twinning, dystocia, stillbirth, abortion, retained placenta and metritis) on the subsequent performance of dairy cows.

Twinning

Cattle (*Bos taurus*) are uniparous species meaning that, in most cases, females produce only one offspring per pregnancy (Komisarek & Dorynek, 2002). Twinning occurs relatively rarely, with the frequency generally not exceeding 1% in most beef herds. However, in dairy herds, the incidence of twin births is higher (on average 3 to 5%), and is strongly affected by age and parity of the dam (Day *et al.*, 1995; Komisarek & Dorynek, 2002; Silva del Río *et al.*, 2007; Ghavi Hossein-Zadeh *et al.*, 2008, 2009). Ghavi Hossein-Zadeh *et al.* (2008) reported parity of dam, season of calving and previous incidence of twinning were potential risk factors for twinning in dairy cows.

The incidence of double births may have both positive and negative effects, which mainly depends on the purpose for which cattle are raised (Komisarek & Dorynek, 2002). A beef cow can wean more total calf weight by raising twins. Twin births offer the potential for increased beef production efficiency, if sustainable changes in management can be made to accommodate problems inherent with twinning (Kirkpatrick, 2002). In addition, increased frequency of twinning would increase the potential for obtaining more progeny from a genetically-superior female, thereby allowing those females to play a larger role in a selection program (Cady & Van Vleck, 1978). The importance of this condition can be expressed along with the application of technologies controlling the sex of calves. In the other words, the use of embryo technologies and sexed semen leads to significantly more female calves (Ghavi Hossein-Zadeh *et al.*, 2010, 2011). This allows dairy producers to select among their herd's potential dams and produce dairy replacement heifers from only the genetically superior animals and promotes enhanced rates of genetic gains (De Vries *et al.*, 2008). However, most authors today would agree that twin pregnancies are undesirable in a dairy herd (Bicalho *et al.*, 2007; López-Gatius *et al.*, 2009; Andreu-Vázquez *et al.*, 2012). However, twin birth is disadvantageous for most beef and dairy producers because of its association with a number of unfavorable effects, including lower potential calf survival, increased culling rate and poorer cow reproductive performance (Fricke, 2001; Bell & Roberts, 2007; Ghavi Hossein-Zadeh *et al.*, 2008, 2010a; Andreu-Vázquez *et al.*, 2012). The risk of pregnancy loss increases and the profitability of the herd diminishes drastically as the frequency of twin births increases (López-Gatius *et al.*, 2002; Lopez-Gatius & Hunter, 2005). One impact of twinning is a reported reduction in the number of fertile heifers available for use as replacements in the dairy herd. This decrease arises from increased neonatal calf mortality of twins and a skewed gender ratio resulting in more homozygous male pairs (Fricke, 2001). Regarding cow performance, twinning is associated with increased dystocia (Ghavi Hossein-Zadeh, 2010b), increased incidence of retained placenta, higher mortality rates, frequent occurrence of freemartins and longer interval from parturition to first estrous (Kirkpatrick, 2002; Echternkamp *et al.*, 2007; Silva del Río *et al.*, 2007). Freemartinism in heifers results from twinning when embryonic membranes of a male and female conceptus fuse during gestation resulting in exchange of blood between the male and female fetuses. Endocrine factors or cells from the male calf cause abnormal development of the reproductive organs of the female calf resulting in infertility. Freemartinism occurs in about 92% of heifers born as a result of heterosexual twin pregnancies (Buoen *et al.*, 1992). Thus, about 8% of heifers from heterosexual twin pregnancies will be fertile, presumably because the fetal membranes fail to fuse or because membrane fusion occurs after the critical period of reproductive organ differentiation (Buoen *et al.*, 1992). Dystocia with twins resulted likely from abnormal presentation of head and (or) legs for one or both twin fetuses at parturition. The increased incidence of fetal malpresentation with twins may result from the higher circulating concentrations of progesterone and estradiol found in cows gestating multiple fetuses (Echternkamp, 1992). Also, cows calving twins are at greater risk for metabolic disorders including displaced abomasum, and ketosis (Fricke, 2001). The presence of twins has been described as the main negative factor of a noninfectious nature affecting pregnancy maintenance (López-Gatius *et al.*, 2002, 2009; López-Gatius & García-Ispierto, 2010). For example, the risk of pregnancy loss during the first trimester of gestation for cows carrying twins is three to nine times higher than for cows carrying singletons (López-Gatius *et al.*, 2002, 2009; López-Gatius & García-Ispierto, 2010). Higher milk production related to twinning is controversial (Beerepoot *et al.*, 1992; Bicalho *et al.*, 2007; Ghavi Hossein-Zadeh, 2010b), and this possible benefit will never outweigh the higher incidence of dystocia, stillbirths, and retained placenta (Beerepoot *et al.*, 1992; Echternkamp & Gregory, 1999). Wiltbank *et al.* (2000) proposed that high milk production increases steroid metabolism as a result of an increased blood flow to the digestive tract and the liver. The subsequent metabolism of the steroid estradiol slows down the natural decline in follicle-stimulating hormone (FSH), which means that follicles have more time to undergo physiological changes before ovulation (Wiltbank *et al.*, 2000). The practical implication of the relationship between milk production and twinning in dairy cattle is important because current dairy-management strategies aim to maximize milk production per cow in the dairy industry. If twinning is related to milk production, this increase would not be unexpected considering the increases in milk production per cow over the years as a result of genetic selection and artificial insemination. Other studies reported a negative association or non-association between milk production and twinning in dairy cattle (Deluyker *et al.*, 1991; Bell & Roberts, 2007). A possible explanation for reduction in milk production after twin calvings was probably due to increase in the incidences of metabolic disorders experienced by cows calving twins during the early stages of lactation. In effect, longer calving to conception intervals and higher culling rates have been reported for cows delivering twins compared with cows delivering singletons (Bicalho *et al.*, 2007). The interval from calving to conception (days open) is a summary measure that is influenced by several factors (*i.e.,* voluntary waiting period, estrus detection rate, conception rate) such that it is an intermediate factor and should not be considered a control point in the management of the incidence of twins. A hypothesis as to how the interval from conception to diagnosis of pregnancy may be associated with the risk of twinning is that twin pregnancies may be more fragile and both pregnancies may be lost if cows are palpated earlier. Under this hypothesis, a positive association between twinning rate and the length of this association would be found because cows pregnant with twins and palpated earlier would be more likely to abort. It is now clear that twin pregnancies reduce herd profitability. The real economic impacts of twinning are probably on the rise because twinning rates have increased considerably over the past 20 yr and estimates currently run at 9%, or even 12% in some herds (Silva del Río *et al.*, 2007). Ghavi Hossein-Zadeh (2010b) observed twins had the lower birth weight than singletons. The reduction in birth weight for twin calves was probably because of the reduced gestation length among cows calving twins (Day *et al.*, 1995; Echternkamp & Gregory, 1999).

Dystocia

Dystocia, more commonly known as difficult calving and defined as prolonged or difficult parturition, is a problem most dairy producers encounter (Mee, 2004, 2008a). There is a wide range of definitions for dystocia ranging from need for assistance to considerable force or surgery to extract the newborn (Mee, 2008a). There are several ways to assess difficulty at parturition (also referred to as calving ease in cattle). Categorical scoring scales that allow for different degrees of difficulty are commonly used across species with ordinal scales with 3 to 5 rating points being popular in cattle (Mee, 2008a). Lower scores are usually given to the easiest births (also called eutocial) and highest scores to the most difficult ones. For example, in the Iran, dystocia evaluations in the Holstein Friesian breed are currently performed using the following 5 point scale: 1 = unassisted, score 2 = slight assistance, score 3 = considerable assistance, score 4 = considerable force needed, and score 5 = caesarian (Ghavi Hossein-Zadeh, 2010). On the other hand, in the UK, genetic evaluations in the Holstein Friesian breed are currently performed using the following 4 point scale: "1 = easy; 2 = assisted; 3 = difficult; 4 = vet assisted" (Eaglen *et al.*, 2011). Because definitions of dystocia vary in the literature, it is not surprising that there is variation in the international prevalence rates of calving difficulty. Internationally, reported prevalence in dairy cattle of severe or considerable difficulty in calving vary from just below 2% to over 22%. However, assistance at calving (including lower degrees of difficulties) is much more prevalent, varying from 10% to over half of the calvings (Mee, 2008a). The evaluation of costs associated with dystocia scores enables dairy producers to predict the average future economic loss when an incident of dystocia is reported in the herd, allowing the producer to evaluate the relative importance of dystocia in individual herds. By realizing the importance of dystocia in a herd, a producer can take appropriate measures to maximize profit, such as selecting sires for calving ease for heifer matings (Dematawewa & Berger, 1997). Dematawewa & Berger (1997) concluded the use of sires that were selected for calving ease for heifer matings could improve economic gains considerably. The total economic costs attributable to a severe case of dystocia have recently been estimated at up to €500 per case (McGuirk *et al.,* 2007).

There are different causes and risk factors associated with dystocia in dairy cattle which can result from both maternal and foetal factors. The most common reason for dystocia results from a physical incompatibility between the pelvic size of the mother and the size of the calf at birth, also called foeto-pelvic incompatibility (or FPI) (Meijering, 1984; Mee, 2008a). This is largely influenced by the weight and morphology of the dam and the calf, respectively. The pelvic area available at birth is affected by the size of pelvis but also by fatness of the dam which might partially obstruct the birth canal. The calf's physical factors contributing to a size mismatch between the calf and the dam may include a calf of a big size or malpresentation. These morphological factors are themselves dependent upon different variables including the age, breed and parity of the dam, twinning, the sex and weight of the calf, the sire and breed of the calf as well as the nutrition of the dam during gestation (Meijering, 1984; Hickson *et al.*, 2006; Mee, 2008a; Zaborski *et al.*, 2009; Ghavi Hossein-Zadeh, 2010b). Dams with low calving weight as well as abnormally low or high body condition score can result in difficulty at parturition as well (Philipsson, 1976b). Adequate body condition score at calving for both primiparous and multiparous dams (BCS of 2.5 to 3, when assessed on a 5 point scale) ensures optimization of ease of delivery and subsequent performance. Primiparous cows are known to have greater risk of difficulty than multiparous cows (Ghavi Hossein-Zadeh, 2010b; Gaafar *et al.*, 2011), partly because of their smaller size and pelvic size. It is recommended that first calving takes place between 22 to 24 months of age to optimize subsequent performance and ease of delivery (Le Cozler *et al.*, 2008; Berry & Cromie, 2009). In order to avoid cases of FPI, it is particularly important for the animal caretaker to mate primiparous animals with bulls that are not expected to sire very large calves. This can be achieved by making an informed choice on their genetic potential for their expected ease of calving. Even if FPI is the major reason leading to difficulty at calving, dystocia can result from other causes that interfere with the expulsive forces needed to expel the calf. This includes: lack of uterine contractions (weak labour), incomplete dilation of the cervix and vagina due to stenosis (narrowing and stiffening of the tissue) and uterine torsion. Risk factors for weak labor include hormonal imbalances such as reduction in plasmatic oestradiol concentration, high levels of oestradiol-17ß at parturition (Sorge *et al.*, 2008) or high ratios of cortisol to progesterone. These imbalances can decrease expression of oxytocin receptors in the uterus as well as changing the preparation of the soft tissues, causing weak uterine contractions and weak dilatation of soft tissues (Sorge *et al.*, 2008). Calving difficulty has a genetic underlying component certainly because many factors that are accounting for FPI are also under genetic control. The genetics of calving difficulty are complex because it is a combination of both maternal effects (also called grandsire effects) and effects from the sire of the calf (also called sire effect or direct effect) (Meijering, 1984).Thus, the sire of the calf partly explains the birth weight of the calf and its morphology. Additionally, variables such as the pelvic size of the dam, the length of gestation and calving weight result partly from the dam's sire. The heritability of calving difficulty (which means the probability of transmission to the following generation) is quite low with estimates of both direct and maternal heritabilities being estimated between 0.03 and 0.20 (Meijering, 1984) but mostly reported below 0.12 in dairy cattle (*e.g.* Steinbock *et al.*, 2003; Eaglen & Bijma, 2009; Eaglen *et al.*, 2010a) and in beef cattle (Bennett & Gregory, 2001; Eriksson *et al.*, 2004). There are negative correlations between direct and maternal effects (Philipsson, 1976a), which means that genetically, a heifer prone to be born easily will be more likely to have difficulty when she calves herself. It is therefore challenging to find the right balance between the ease with which a cow calves and with which her female offspring will herself calve when she reaches adulthood. This result is also controversial and has not been found consistently across populations (Eaglen & Bijma, 2009). High genetic correlations are also observed for calving difficulty between first and later parities (Carnier *et al.*, 2000; Eriksson *et al.*, 2004). This means that similar genes and mechanisms may be involved in both parity levels and that some cows may be more genetically predisposed to dystocia. However, the heritable variance explains only 10% of the phenotypic variance (Eaglen & Bijma, 2009). As a consequence, although selection against difficult calving is possible and should be encouraged, non-genetic factors (called environmental factors) are also of great importance in the implementation of preventive measures against dystocia (Barrier, 2012).

In the most severe cases, dystocia can lead to the death of the cow, usually occurring within 48 hr (Dobson *et al.*, 2008). Even beyond those 48 hr, cows that have experienced dystocia are more likely to die or be culled in early lactation and over the lactating period (Dematawewa & Berger, 1997; Tenhagen *et al.*, 2007; López de Maturana *et al.*, 2007b; De Vries *et al.*, 2010). Furthermore, the fear that the animal might experience difficulty at her next parturition may increase weight to the farmer's decision to cull a dystocial cow. Cows experiencing difficulty at birth are more likely to suffer from postpartum diseases such as metritis, retained placenta and milk fever (Benzaquen *et al.*, 2007). This could be explained by the possibility of microbial contamination during assistance (Dohmen *et al.*, 2000) combined with a depressed immune status during the peripartum period. This highlights the importance of good hygiene when intervention at calving is required. Immunodeficiency is probably enhanced in dystocial cows as a consequence of the increased duration of labour and the subsequent higher cortisol levels (Civelek *et al.*, 2008). Nakao & Grunert (1990) studied the adrenocortical function of beef cows through adrenocorticotropic hormone (ACTH) challenge postpartum for different degrees of calving difficulty. They found higher reactivity of the hypothalamic-pituitary-adrenal axis for cows having experienced severe dystocia. They suggest that this could increase the susceptibility of the uterus to infection through the anti-inflammatory action of corticosteroids. As well, this might be responsible for causing temporary metabolic disturbances in cows and delaying ovarian recovery and uterine involution. As hormones involved in reproductive function closely interact with hypothalamic-pituitary-adrenal axis regulation, this can be related to impaired fertility. In fact, a prolonged second stage of labour resulted in depressed reproductive performance in both beef and dairy cattle (Dobson *et al.*, 2001). An increase in the number of days open, the number of services to conception and a delay to first service has been shown after dystocia (Dobson *et al.*, 2001; López de Maturana *et al.*, 2007a). This impaired fertility after dystocia is thought to contribute to 30% of the cow related costs of dystocia (Dematawewa & Berger, 1997).

It has been shown that calving difficulty reduces milk yield in the cow. It is not clear however, how long the adverse effect on milk production lasts for. In fact, although some authors seem to find a deleterious effect on the overall lactation of cows (Dematawewa &

Berger, 1997; Ghavi Hossein-Zadeh, 2013), some studies have suggested that these effects disappear beyond 14 days in milk (DIM) (Rajala & Gröhn, 1998), 90 DIM (Thompson *et al.*, 1983) or six month postpartum (Tenhagen *et al.*, 2007). Furthermore, the degree of difficulty from which milk losses are reported ranges from slight degrees of difficulty (Dematawewa & Berger, 1997) up to only in severe cases when surgery is needed (Tenhagen *et al.*, 2007). Additionally, the magnitude of losses has been suggested to be greater with increasing degrees of difficulty (Dematawewa & Berger, 1997). However, the pattern with which milk losses vary is not always obvious and other factors such as the overall yield or parity of the cow (Rajala & Gröhn, 1998) might influence it. As well, it is common for studies looking at milk production losses after a difficult calving to restrain their datasets to animals with full lactations or that have survived until a certain lactation stage.

During the lactating period, dry matter intake was shown to decrease in cows that had experienced dystocia in the months postpartum (Bareille *et al.*, 2003) compared to cows that calved normally, but this was not seen in the first two days postpartum (Proudfoot *et al.*, 2009). This could relate to lower milk production observed in dystocial animals but also to the greater losses in weight and body condition score found in dystocial cows during their subsequent lactation (Berry *et al.*, 2007). According to the authors, this may be related to changes in the metabolic function and lower immunocompetency in these animals (Barrier, 2012). To that extent, the experience of dystocia in Holstein dairy cows is also associated with haematological changes at delivery relating to hepatic function. For example, dystocial Holstein heifers had higher cortisol, cholesterol, glucose, high density lipoprotein (HDL), triglycerides, creatinine and vitamin A levels than eutocial animals, which might reflect higher calving stress in these animals (Civelek *et al.*, 2008). It is possible that such stress but also exhaustion, pain and human intervention during delivery may contribute to reduced or delayed maternal care of the calves in the first hours postpartum, as observed in ewes (Dwyer *et al.*, 2001; Fisher & Mellor, 2002).

At birth, having to make the transition from foetal life to extra-uterine life is a challenging experience in mammals. Animals born from difficult births are more likely to fail that transition and become stillborn or die within the few days of life (Meyer *et al.*, 2001; Johanson & Berger, 2003; Berglund *et al.*, 2003; Eriksson *et al.*, 2004). Within the group of calves that die perinatally, 90% would be alive at the start of the calving process and three quarters of the deaths occur within an hour of birth (Mee, 2008b,c), thus emphasizing how critical the birth process and early hours of life can be. Dystocial stillbirths usually result from internal and external trauma (Berglund *et al.*, 2003; Aksoy *et al.*, 2009) but also from prolonged hypoxia (deprivation of adequate oxygen supply) (Meijering, 1984; Mee, 2008c). There are also concerns about the beef and dairy calves that survive the birth process. Indeed, survival is not just compromised in the perinatal period but there is also evidence that their survival can be affected in the neonatal period (Lombard *et al.*, 2007) and for their lifetime for the more severe degrees of difficulty (Henderson *et al.*, 2011). In the neonatal period, severe hypoxia and acidosis (Alonso-Spilsbury *et al.*, 2005; Civelek *et al.*, 2008), impaired breathing (Breazile *et al.*, 1988) and internal injuries (Berglund *et al.*, 2003; Gundelach *et al.*, 2009; Mee, 2010) may contribute to low vigour (Riley *et al.*, 2004) and subsequent poor survival. Additionally, dystocial calves may not thermoregulate properly (Bellows & Lammoglia, 2000) and achieve lower passive immunity. This may relate to higher morbidity (Steenholdt & Hernández, 2004; Lombard *et al.*, 2007) and possibly altered growth (Goonewardene *et al.*, 2003). Furthermore, it is likely that the experience of difficulty at birth may have long-term effects on heifer calves. It is well-known that the early life experiences can have longterm implications for the performance, cognition, health and welfare of the individuals among diverse species including ruminants and cattle (Vinuela-Fernández *et al.*, 2007). Recently, evidence has emerged from retrospective studies that dystocia could also have potentially long-term effects on dairy heifers. Reduction in survival rates and milk production were seen when they reach an adult age (Eaglen *et al.*, 2010b; Heinrichs & Heinrichs, 2011; Henderson *et al.*, 2011). There are many potential threats to achieving good standards of welfare for the dam and her calf (or calves) after a difficult calving. These include pain during parturition as a result of calving injuries, painful health conditions, injuries at birth but also distress following poor health, breathlessness, hypoxia and potential hypothermia. These in turn might result in poor production and survival. Possible long-term alteration of the development of the dairy calves following birth difficulty is also likely (Barrier, 2012).

Abortion

Abortion in dairy cattle is commonly defined as a loss of the fetus between the age of 42 days and approximately 260 days (Peter, 2000). The diagnosis of abortions often presents a challenge to the herd owner and the herd veterinarian. Although a gradual increase in the abortion rate in a herd may be noted over a period of many years, a sudden and dramatic increase is more commonly seen. For this reason, prompt and thorough action is required when abortions do occur. Well kept records will often be of benefit during the investigation of abortion problems. Breeding dates, parity, production information and health events (*e.g.,* disease or vaccination) can all help to identify factors which may be associated with the abortions. Other herd level information such as ration changes, new additions, personnel changes, etc., should also be recorded. This kind of information should be kept in a readily accessible format on all dairy farms and will serve many functions in addition to being useful for investigating abortion problems.

Abortions represent a loss of reproductive efficiency in normal bovine populations and spontaneous abortion of dairy cows is an increasingly important problem that contributes substantially to low herd viability and production inefficiency by reducing the number of potential female herd replacements and lifetime milk production, and by increasing costs associated with breeding and premature culling (Thurmond *et al.*, 2005). Fetal mortality for cows confirmed pregnant between 35 and 45 days of gestation typically has ranged from 8 to 10% (Forar *et al.*, 1996), with abortion often exceeding 14% in some herds (Thurmond *et al.*, 1990; Ghavi Hossein-Zadeh *et al.*, 2008). While infectious diseases are a primary focus of abortion prevention, infectious agents probably cause less than half of the fetal deaths. The cost of abortion varies according to such effective factors as the time of gestation, milk production, days in milk, the time of insemination after parturition, the cost of nutrition, sperm costs, insemination time, and labor costs, which differ from region to region (Rafati *et al.*, 2010). Abortions during early pregnancy result in increased days open. Following late term abortions, there is a loss of potential replacement heifers. These late term abortions often result in early culling of productive cows. Moreover, extended calving intervals reduce production. Increasing the calving interval from 12 to 13 months may result in a loss of 2-5% of the herd's potential calf production. Calving intervals over 14 months will produce loss of greater than 10% in average producing dairy herds. Often the causes of these abortions are very difficult to determine resulting in a lot of frustration for the dairymen and their veterinarians. Expect that only 30-50% of submissions to veterinary diagnostic laboratories will yield a definitive diagnosis. Most dairies experience an observable abortion rate of from 2-5% yearly. Despite ongoing research investigations to diagnose and evaluate the epidemiology of infectious factors that cause abortion, breeders are still confronted with abortion continuously. Hovingh (2009) listed numerous causes of abortion: infectious agents (bacteria, viruses, protozoa, and fungi), toxic agents, heat stress, and genetic abnormalities. Twin pregnancies (Nielen *et al.*, 1989) and mastitis (Santos *et al.*, 2003) have also been implicated. Infectious agents are the most commonly diagnosed cause. Jamaluddin *et al.* (1996) examined 595 abortion submissions in California and found that infectious agents accounted for 37.1%; noninfectious agents, 5.5%; and undetermined causes, 57.3%. Among the 37.1% due to infectious agents, bacteria accounted for 18.0%; protozoa, 14.6%; viruses, 3.2%; and fungi, 1.3%. In Canada, Khodakaram-Tafti & Ikede (2005) indicated that the three most common identifiable infectious agents were bacterial (24%), fungal (7%), and viral (6%). Several recessives detrimental to reproductive performance have been confirmed and documented for several dairy breeds. An example of a genetic abnormality that causes abortion is the complex vertebral malformation (CVM) gene in Holsteins (Agerholm *et al.*, 2001). The CVM gene causes malformations in middle to late gestation. However, most of these infectious factors have been brought under control by appropriate vaccination. Moreover, successful etiology diagnosis of abortion shows less than half of the fetal death (Geoffrey *et al.*, 1992; Markusfeld-Nir, 1997; Thurmond *et al.*, 2005). Non-infectious factors include genetic and non-genetic disorders that have been reported in some investigations. Heat stress, production stress, and other unfavorable conditions including seasonal effect and season changes, especially summer are the most important non-genetic factors (Labernia *et al.*, 1996; Markusfeld-Nir, 1997; Hansen, 2002; López-Gatious *et al.*, 2002; Bitaraf Sani & Amanloo, 2007). Genetic disorders include chromosomal and single gene disorders. Contrary to human chromosomal disorders, which result in about 50% abortion, in farm animals the rate is lower, but a sterile calf can result (Geoffrey *et al.*, 1992).

Mutation in codon 405 of the uridine monophosphate synthase (UMPS) gene is the putative example of single gene disorders (Fries & Ruvinsky, 1999). Different non-infectious maternal and paternal factors have been reported for fetal death; for example cow parity (Lee & Hwa Kim, 2007), sire effect (Markusfeld-Nir, 1997), age at conception (Thurmond *et al.*, 1990, 2005; Hanson *et al.*, 2003), and abortion history (Hanson *et al.*, 2003; Thurmond *et al.*, 2005). In a study on Iranian Holsteins, Ghavi Hossein-Zadeh & Ardalan (2011a) reported normal-calved cows had greater 305-d milk production, fat yield and protein yield of milk than abortive-calved cows. But abortive-calved cows had the greater milk fat percentage than normal calved cows. Also, they observed that the risk of abortion was higher at the 5th month of pregnancy for parities 1 and 2, but this risk was greater at the 4th month of pregnancy for cows in their third parity or beyond. Thurmond *et al.* (1990) reported the greatest risk of fetal loss is during the first trimester of gestation and then progressively decreases as gestation advances with a slight increase in the risk toward the last month of gestation. Forar *et al.* (1996) reported the cumulative incidence of fetal loss between 31 and 260 days of gestation is 10.8%. Of this only 20% of the fetal losses are detected by observation of an expelled fetus or fetal membranes and the proportion detected increases with increasing gestational age at time of fetal loss. Thurmond *et al.* (2005) reported the predicted probability of abortion increased with increasing dam age at conception, with increasing number of previous abortions, and if the previous pregnancy was aborted > 60 days in gestation. Also the predicted probability of abortion decreased with increasing number of days open.

Continued increases in milk production over the last two decades in dairy herds have been concurrent with an increase in abortion rate over the years so that Ghavi Hossein-Zadeh *et al.* (2008) reported there was increasing trend for the odds of abortion over the years in Iranian Holsteins. Also, they observed that greater odds of abortion existed for singleton births and cows in their fourth and greater lactations than other parities. Previous studies reported the greater abortion rates for twin calves than singleton calves (Guerra-Martinez *et al.*, 1990; Day *et al.*, 1995; Echternkamp & Gregory, 1999), but Mee (1991) reported the abortion frequencies being 1.81% and 1.20% for single and twin births, respectively. Bartels *et al.* (2006) reported 0.72 kg d^{-1} decrease in milk production during the first 100 days of lactation in the first year after the abortion epidemic in Dutch dairy herds. Hanson *et al.* (2003) and Thurmond *et al.* (2005) observed the higher number of days open decreases the risk of abortion. Uterine involution in cows due to previous pregnancy's outcome (successful parturition, dystocia, retained placenta and abortion) is different. Inhospitable uterine environment seen in dairy cows as a result of common problems such as endometritis and retained placenta increase the risk of abortion (Hanson *et al.*, 2003). Additionally, in the first two to three months of production cows are faced with negative energy balance, especially those with high milk yield (Ghorbani & Asadi-Alamoti, 2004). They lose weight during this period which can cause a reduction in body condition score with a corresponding negative correlation with progesterone secretion, harmful to fetal survival (Grimard *et al.*, 2006). Aborted cows are at 3.2 times higher risk of being culled; however, only 1 out of 6 are recorded as "culled for abortion". Aborted cows if not culled have 5 times more likely to abort subsequently than cows that never aborted. If one calculates the conception to conception interval, it is 173 days on an average. On average it takes 72 days for a cow to conceive after an abortion, however, there is a gestation age effect. As gestational age increased, time to rebreed increased. In the first trimester abortion it took 54 days to rebreed and 85 days in the second semester abortion and 116 days in the third semester abortion. The basis of cost estimation is to determine the number of days open plus the gestational days at the time of abortion. It can range from 150 to 225 days or more for a herd. Cost of open day estimate can be used to obtain the loss and inclusion of veterinary intervention and medication can provide the total loss due to abortion (Peter, 2000).

Stillbirth

Stillbirth was defined as a calf loss from day 260 until the end of normal gestation period. Trait definitions vary slightly between countries, with most defining stillbirths as those calves born dead or dying within 24 h of parturition (Philipsson *et al.*, 1979), although Germany and the United States include deaths within 48 h of birth (Berger *et al.*, 1998). Breed differences play a role in perinatal mortality (Philipsson, 1976b), and Rossoni *et al.* (2005) reported that 10% of Italian Brown Swiss calves did not suckle by the third meal offered postpartum, contributing to increased postnatal mortality. Incidence rates and heritabilities were similar when comparing parities across countries despite differences in trait definition, with the exception of Sweden (Steinbock *et al.*, 2003). The overall incidence of calf stillbirth in Holstein cows of Iran was reported to be 4.9% and varied among herds from 2.9 to 9.8% (Ghavi Hossein-Zadeh *et al.*, 2008). The incidence of stillbirth parturition in dairy cows seems to have increased in recent years (Meyer *et al.*, 2000, 2001; Hansen *et al.*, 2004; Bicalho *et al.*, 2007; Ghavi Hossein-Zadeh *et al.*, 2008). During the past 20 years an increase from about 6 to 10.3% has occurred in the incidence of stillbirth in the USA (Berglund *et al.*, 2003). Meyer *et al.* (2001) reported the percentage of stillborn calves in primiparous cows increased from 9.5% in 1985 to 13.2% in 1996 and increased from 5.0% to 6.6% from 1985 to 1996 for multiparous cows. Hansen *et al.* (2004) reported the overall frequency of stillbirth in Danish Holsteins increased from 0.071 to 0.090 during 1985 to 2002. The great variation in the incidence of stillbirth by farm suggests that management practices (breeding, genetic selection, husbandry, etc.) adopted by individual farms may influence the incidence of stillborn calves (Bicalho *et al.*, 2008). Ghavi Hossein-Zadeh *et al.* (2008) observed greater odds of stillbirth existed for calves born from primiparous cows than from multiparous cows and for calves born as twins than singletons. Hansen *et al.* (2004) cited that the higher incidence of stillbirth in first-parity cows was due to the disproportion between the size of the calf and the dam's pelvis, which caused difficult calvings. Meyer *et al.* (2000) reported that calving difficulty, gestation length of 15 to 12 d below the mean, and male calves were important risk factors for stillbirth. Bicalho *et al.* (2007) and Meyer *et al.* (2001) reported a significant decreasing trend in the incidence of stillbirth by parity in Holstein dairy cows. Also, different studies indicated that male calves had significantly more stillbirths than heifer calves (Mee, 1991; Heins *et al.*, 2006; Ghavi Hossein-Zadeh *et al.*, 2008). This effect is probably due to greater body size of male calves than female ones at birth. The economic loss due to lost calves increased from 1985 to 1996 due to the increase in incidence of stillbirths from 9.5 to 13.2% in primiparous and 5.0 to 6.6% in multiparous cows (Meyer *et al.*, 2001). The economic loss is even greater if the detrimental effects of stillbirth on the dam's lactation performance are considered. Stillbirths were associated with increased risk of developing metritis and retained placenta (Emanuelson *et al.*, 1993), and with decreased risk of conception (Maizon *et al.*, 2004). Stevenson & Call (1988) reported that cows experiencing stillbirths were at increased risk for a number of postpartum disorders such as prolapsed uterus, retained placenta, metritis, and displaced abomasum. Correa *et al.* (1993) also reported increased odds of developing metritis and retained placenta for cows that had stillbirth. It is possible that the higher incidence of postpartum disorders may decrease the survival of cows that had stillbirths. Also, it is likely that the dead calf inside the uterus is accelerating intrauterine bacterial growth which would cause metritis. Furthermore, retained placenta and metritis have been associated with decreased milk yields. Bicalho *et al.* (2007) observed that cows with stillbirth were at a 41% increased hazard to die or to be culled from the herd than cows without stillbirth. Analyzing a large data set from the Quebec Dairy Herd Analysis Service, Mangurkar *et al.* (1984) reported that perinatal deaths led to higher culling rates due to lower milk production and impaired reproductive performance when compared to normal calvings. Few studies have attempted to determine the effects of stillbirth calvings on the dam's subsequent survival and days open. Mangurkar *et al.* (1984), using a mixed linear model statistical procedure, reported that cows that gave birth to stillborn calves had increased risk of being culled and less chance of getting pregnant. Bicalho *et al.* (2007) reported stillbirths significantly increased the risk of death/culling throughout the lactation. Cows that gave birth to stillborn calves had a 40.9% higher hazard rate of death/culling compared with cows that gave birth to live calves. Mangurkar *et al.* (1984) reported a milk loss from perinatal deaths of 100-400 kg of milk, 4-11.5 kg of fat, and 2.5-13 kg of protein. Bicalho *et al.* (2008) estimated daily milk loss was 1.1 kg which is equivalent to 335.5 kg for a 305-day lactation. A review of the literature by Fourichon *et al.* (1999), reported that out of the five publications reviewed two papers reported no effect, and three papers reported a detrimental effect of stillbirth calvings on milk production. Milk losses attributed to stillbirth calvings were much higher in the beginning of the lactation and by the 9th month of lactation there was little apparent milk loss (Bicalho *et al.*, 2008). Atashi (2011) concluded that stillbirth significantly decreased milk and fat yields in Iranian Holsteins (loss of 591.43 ± 69.19 kg milk and 13.77 ± 2.57 kg fat per cow per lactation). The biology of how stillbirth calvings may affect milk production is thus far unknown. As mentioned by Mangurkar *et al.* (1984), it is possible that stillbirth initiates a cascade of effects that will detrimentally affect the cow's performance, but it is also possible that there are common causes to calf mortality and dams' poor performance. For instance, in humans maternal obesity is a well known risk factor for stillbirth; obese pregnant women are at 2.1 times higher odds of having stillbirths when compared to normal weight pregnant woman (Chu *et al.*, 2007). Chassagne *et al.* (1999) reported that body-condition score ≥ 4 was an important risk factor for stillbirth. Furthermore, heifers are at a greater risk of been over conditioned around parturition than adult cows; hence, heifers are at higher risk for stillbirth parturitions than older cows (Hansen *et al.*, 2004; Bicalho *et al.*, 2007). Obese heifers are potentially more susceptible to dystocia, ketosis, and other metabolic diseases. Circulating neutrophils play an important role in the rejection of the placenta and in uterine defense in the postpartum; the prepartum circulating neutrophil count for heifers that experienced stillbirth parturition was lower than for heifers that did not have stillbirth (Chassagne *et al.*, 1999). In these scenarios, stillbirth would be confounded with the effect of over-conditioning heifers on milk production and therefore would not be a true cause of decreased milk production.

Stillbirth has been shown to be heritable (Philipsson, 1976b; Ghavi Hossein-Zadeh, 2011) and this means that stillbirth is a potential trait to include in a breeding program. Hansen *et al.* (2004) reported an unfavorable trend of direct and maternal genetic effects for stillbirths in the Danish Holstein population. In that study, the use of Holstein Friesian sires was the main cause for the increased stillbirth incidence. One of the best management practices to reduce stillbirth parturition may be utilizing sire and daughter calving ease information when selecting sires to breed heifers. Herd managers should review calving procedures with their veterinarian to assure that proper timing and calving assistance techniques are used when providing assistance during parturition. In addition, providing a good environment for heifers and cows to minimize stress before parturition can reduce stillbirth incidence (Atashi, 2011).

Retained placenta and metritis

Diseases mainly affect dairy cow productivity in three ways: 1) by reducing reproductive efficiency, 2) by shortening the expected length of productive life (*i.e.,* by increasing culling risk), and 3) by lowering milk yield (Rajala & Gröhn, 1998). Numerous studies (*e.g.,* Erb *et al.*, 1985; Gröhn *et al.*, 1990) have shown that diseases related to the reproductive tract (dystocia, retained placenta, and metritis) are interrelated and can affect the length of calving interval, the number of days open, and the reproductive efficiency in general. These diseases can also affect the overall productivity of dairy cows by reducing milk yield. A cow was considered to have retained placenta (RP) when the fetal membranes were visible at the vulva or were identified in the uterus or vagina by vaginal examination more than 24 h after the first observation of the cow or heifer following calving. The condition of retained placenta occurs in 4 to 18% of calvings (Markusfeld, 1987; Esslemont & Kossaibati, 1996). Ghavi Hossein-Zadeh & Ardalan (2011b) reported the mean frequency of retained placenta ranged from 3.5% in first lactation to 6.9% in third lactation cows. In the USA, RP was reported to be the third most common health disorder in dairy cows, affecting 7.8% of lactating cows (Goff, 2006). Calving problems including dystocia (Gröhn *et al.*, 1990; Correa *et al.*, 1993; Emanuelson *et al.*, 1993), stillbirths (Markusfeld, 1987; Correa *et al.*, 1993), and multiple births (Markusfeld, 1984; Correa *et al.*, 1993) are associated with an increased incidence of retained placenta. In addition to these problems, abnormalities in partus, parity (Markusfeld, 1984; van Werven *et al.*, 1992), gestation length (Muller & Owens, 1974; Markusfeld, 1984), calving season (Muller & Owens, 1974; Markusfeld, 1984), and nutrition (Laven & Peters, 1996) are also considered risk factors for retained placenta. Ghavi Hossein-Zadeh & Ardalan (2011c) reported abortion was the most important risk factor for RP and other risk factors for RP were dystocia, stillbirth, milk fever, twin births, pluriparity, winter season and shorter gestation length of dairy cows in Iran. However, some researchers have found no association between dystocia (Erb *et al.*, 1985), cow parity (Muller & Owens, 1974), or calving season (Grohn *et al.,* 1990) and the incidence of retained placenta.

Rajala & Gröhn (1998) reported retained placenta had a significant negative effect on milk yield for several weeks after calving, which is in agreement with results of several other studies. Lucey *et al.* (1986) found that retained placenta suppressed milk yield for about 4 wk after calving, and Rowlands & Lucey (1986) reported that retained placenta reduced peak yield, but also had a more lasting negative effect. They estimated a 7% reduction in 305-d yield for cows with retained placenta. In the study of van Werven *et al.* (1992), older cows showed decreased milk yield with an increase in the duration of retention of the placenta. Simerl *et al.* (1992) found milk yield in first lactation to be depressed by retained placenta. Deluyker *et al.* (1991) reported that retained placenta was followed by lowered mean values for yield during the first 5 d after calving. Martin *et al.* (1986), however, found no yield effect from retained fetal membranes. They used 305 d milk yield as their milk measure. The indirect negative effect of RP on milk yield mediated by puerperal metritis is reported by Könyves *et al.* (2009).

Retained placenta, one of the main causes of endometritis in cattle, causes economic loss (Kaneene & Miller, 1995). Kossaibati & Esslemont (1997) calculated the direct cost of a case of retained placenta to be about €96.34, with an over-all cost of €346.24. Many, often interrelated, factors have been implicated in the occurrence of retained placenta (Laven & Peters, 1996). Retained placenta is a direct risk factor for postpartum reproductive and metabolic disorders (Chassagne *et al.*, 1999), which may affect subsequent reproductive capability of dairy cows. In fact, a negative impact of retained placenta on reproductive performance of dairy cows has been widely documented (Fourichon *et al.*, 2000; Gröhn & Rajala-Schultz, 2000). However, others have reported that retained placenta does not significantly alter fertility (Kaneko *et al.*, 1997). Increased occurrence of retained placenta in cows with abnormal partus might be due to lack of tone and slow involution or damage to the uterus by mechanical stress resulting from calving difficulty (Markusfeld, 1984; Markusfeld, 1987). Previous reports (Markusfeld, 1984, 1987; Chassagne *et al.*, 1999) on the relationship between gestation length and the incidence of retained placenta showed that shorter gestation lengths are associated with a higher incidence of retained placenta. Han & Kim (2005) demonstrated that retained placenta was an important predisposing factor for development of postpartum endometritis and metabolic disorder in dairy herds, as previously reported by others (Markusfeld, 1986). The condition of the uterus at parturition or soon after may determine whether potential pathogens cause infections. At this time, retained placenta (a perfect media for bacterial growth), dystocia, or involution characteristics of the cervix and uterus may predispose cows to various infections (Bruun *et al.*, 2002). Thus, the relationship between retained placenta and endometritis should be considered carefully; a large proportion of primary endometritis cases occurred just after the occurrence of retained placenta (Markusfeld, 1984). Erb *et al.* (1985) found an indirect association between the occurrence of ovarian cyst and retained placenta mediated by endometritis. Han & Kim (2005) reported the occurrence of metabolic disorder (abomasal displacement, milk fever, or ketosis) was greater in the retained placenta group than in the control group. Cows with retained placenta have previously been reported to have a higher incidence of abomasal displacement and ketosis (Markusfeld, 1987) compared to cows without retained placenta, although one report did not find a relationship between retained placenta and abomasal displacement (Correa *et al.*, 1993). Retained placenta has been suggested to reduce fertility in two ways: first, by a direct effect through an unknown mechanism and secondly, by an indirect effect through endometritis (Stevenson & Call, 1988; Laven & Peters, 1996). Han & Kim (2005) reported the intervals from calving to first service and conception were higher in the retained placenta group than in the control group, which is consistent with other reports (Ouweltjes *et al.*, 1996). In some studies, however, the intervals from calving to first service and/or conception were not related to the occurrence of retained placenta (Coleman *et al.*, 1985; Kaneko *et al.*, 1997). RP increases the risk of fatty liver syndrome and ketosis (Han & Kim, 2005); the latter, in turn, delays the postpartum resumption of cyclic ovarian function and prolongs the interval from calving to first ovulation (Opsomer *et al.*, 2000). Könyves *et al.* (2009) observed negative energy balance (NEB) developing at the end of gestation markedly increased the odds of developing RP. Hur *et al.* (2011) concluded that there is a very close relationship between RP and postpartum diseases in dairy cattle after calving and RP increases risks for postpartum diseases such as metritis and mastitis, and culling hazards up to 60 DIM. Gaafar *et al.* (2010) observed retained placenta resulted in an increase in the period from parturition to first estrus (25.90 *vs.* 20.50 days) and first service (56.90 *vs.* 47.20 days), service period (57.70 *vs.* 46.10 days), days open (106.90 *vs.* 92.70 days), number of services per conception (3.50 *vs.* 2.60) and calving interval (395.20 *vs.* 372.90 days). Moreover, they observed reduction in conception rate (66.70 *vs.* 74.10%) and average daily milk yield (13 *vs.* 14 kg) compared to normally calved cows.

Metritis (MET) is inflammation of the uterus resulting in systemic signs of sickness, including fever, red-brown watery foul-smelling uterine discharge, dullness, inappetance, elevated heart rate, and low production (Sheldon *et al.,* 2006). Ghavi Hossein-Zadeh & Ardalan (2011b) reported the mean frequency of MET ranged from 6.6% in first lactation to 9.6% in third lactation cows of Iran. Also, Ghavi Hossein-Zadeh & Ardalan (2011c) indicated risk factors for MET included RP, dystocia, stillbirth, twin births, primiparity, winter season and male calves in Iranian Holsteins. Metritis in dairy cows is an important disease, because it can increase the calving to conception interval (Erb *et al.,* 1981; Fourichon *et al.*, 2000) and decrease milk yield (Coleman *et al.,* 1985). Also, cows with severe metritis ate 2-6 kg dry matter less than healthy cows in the 2-3 weeks preceding the clinical signs of metritis (Huzzey *et al.,* 2007), and to negatively affect reproductive performance (Opsomer *et al.*, 2000; Melendez *et al.*, 2004). The largest risk factor for metritis is RP, but other conditions that may impair feed intake and immune function also increase the risk of metritis (LeBlanc, 2008). Some discrepancy exists in the literature about the effect of metritis on milk yield. Some studies have reported decreased yield (Deluyker *et al.*, 1991; Simerl *et al.*, 1992; Rajala & Grohn, 1998), but others show no or equivocal effects of the disease on yield (Goshen & Shpigel, 2006). This discrepancy may be partially explained by differences in parity. Østergaard & Gröhn (1999) found that multiparous cows, but not primiparous cows, with metritis produced less milk than healthy cows up to 6 wk after diagnosis. This parity effect has remained unexplained, but may be due to differences in feed intake. Huzzey *et al.* (2007) found that ill cows consumed less feed than healthy cows; yet, this has not been tested in primiparous and multiparous cows separately. Metritis and other infections of the reproductive tract can harm reproductive performance (Sheldon *et al.*, 2006). Cows with metritis have increased days between first service after calving and conception, increasing the efforts and resources required to induce pregnancy (Erb *et al.*, 1981; Fourichon *et al.*, 2000). Reproductive status is the most important influence on culling decisions (Grohn *et al.*, 2003), so it seems likely that uterine infections increase the risk of culling. Wittrock *et al.* (2011) demonstrated that metritis reduces acute feed intake, long-term milk yield, and increases the chance of culling in multiparous cows but not primiparous cows. Metritis decreased daily milk production from 2 to 13 kg during a period that can vary from 2 to 20 wk after parturition (Rajala & Grohn, 1998; Fourichon *et al.*, 1999; Wittrock *et al.*, 2009). The effect of metritis on milk production was reported to be influenced by parity and stage of lactation (Overton & Fetrow, 2008; Wittrock *et al.*, 2009). The reported effect of uterine diseases on culling is variable. Some studies found an increased risk of culling (Overton & Fetrow, 2008), whereas others found no effect (Grohn *et al.*, 2003). Disease definition, duration of the follow-up period, sample size (power), and accounting for related diseases are important factors contributing to this discrepancy. In studies in which uterine diseases increased culling, this was suggested to be the result of either decreased milk production or reduced reproductive performance (Grohn & Rajala-Schultz, 2000; Overton & Fetrow, 2008). Dubuc *et al.* (2011) reported uterine disease decreased pregnancy rate, which was a substantial risk factor for culling; however, if affected cows became pregnant they were not at greater risk of culling. Also, in a study on Danish Holsteins, Elkjær *et al.* (2013) reported cows with metritis in early lactation presented a significant delay in first insemination (hazard ratio of 0.80) and a significantly reduced probability of success at first insemination.

Conclusions

There appears to be an agreement in the literature that health and reproductive problems mentioned in the current paper have adverse effects on the health, production and reproduction indices of the dairy cow. Because the current goal of dairy operations is to maximize milk yield per cow through genetic selection and artificial insemination, the practical implication of the association between health problems and milk production and identification of potential risk factors for corresponding problems in dairy cattle is substantial. Development of practical management strategies to cope with the negative effects associated with reproductive and health problems on dairies is critical. Because health and reproductive problems mentioned in the current study are the most important conditions that limits cow's performance and considerably erode the profit, maintaining the general health and immune function of the cattle is also important in minimizing the risk of health problems. Providing an adequate amount of a properly formulated and delivered ration, and providing a clean, comfortable and minimal-stress environment is also essential to accomplishing this task.

References

Agerholm JS, Bendixen C, Andersen O, Arnbjerg J, 2001. Complex vertebral malformation in Holstein calves. J Vet Diagn Invest 13: 283-289.

Aksoy O, Ozaydin I, Kilic E, Ozturk S, Gungor E, Kurt B, Oral H, 2009. Evaluation of fractures in calves due to forced extraction during dystocia: 27 cases (2003-2008). Kafkas Univ Vet Fak Derg 15(3): 339-344.

Alonso-Spilsbury M, Mota-Rojas D, Villanueva-García D, Martínez-Burnes J, Orozco H, Ramírez-Necoechea R, López Mayagoitia A, Elena Trujillo ME, 2005. Perinatal axphyxia pathophysiology in pig and human: a review. Anim Reprod Sci 90: 1-30.

Andreu-Vázquez C, García-Ispierto I, Ganau S, Fricke PM, López-Gatius F, 2012. Effects of twinning on the subsequent reproductive performance and productive lifespan of high-producing dairy cows. Theriogenology 78: 2061-2070.

Atashi H, 2011. Factors affecting stillbirth and effects of stillbirth on subsequent lactation performance in a Holstein dairy herd in Isfahan. Iran J Vet Res 12: 24-30.

Bareille N, Beaudeau F, Billon S, Robert A, Faverdin P, 2003. Effects of health disorders on feed intake and milk production in dairy cows. Livest Prod Sci 83(1): 53-62.

Barrier AC, 2012. Effects of a difficult calving on the subsequent health and welfare of the dairy cows and calves. PhD Dissertation, University of Edinburgh, UK.

Bartels CJM, Van Schaik G, Veldhuisen JP, Van den Borne BHP, Wouda W, Dijkstra T, 2006. Effect of *Neospora caninum-serostatus* on culling, reproductive performance and milk production in Dutch dairy herds with and without a history of *Neospora caninum*-associated abortion epidemics. Prev Vet Med 77: 186-198.

Beerepoot GMM, Dykhuzen AA, Nielen M, Schukken YH, 1992. The economics of naturally occurring twinning in dairy cattle. J Dairy Sci 75: 1044-1051.

Bell MJ, Roberts DJ, 2007. Effect of twinning on the feed intake, performance and health of dairy cows. Livest Sci 107: 274-281.

Bellows RA, Lammoglia MA, 2000. Effects of severity of dystocia on cold tolerance and serum concentrations of glucose and cortisol in neonatal beef calves. Theriogenology 53(3): 803-813.

Bennett GL, Gregory KE, 2001. Genetic (co)variances for calving difficulty score in composite and parental populations of beef cattle: I. Calving difficulty score, birth weight, weaning weight, and postweaning gain. J Anim Sci 79(1): 45-51.

Benzaquen ME, Risco CA, Archbald LF, Melendez P, Thatcher MJ, Thatcher WW, 2007. Rectal temperature, calving-related factors, and the incidence of puerperal metritis in postpartum dairy cows. J Dairy Sci 90(6): 2804-2814.

Berger PJ, Thompson JR, Sattler CG, 1998. Preliminary investigations on the feasibility of a stillbirth evaluation for the USA. Interbull Bull 18: 28-30.

Berglund B, Steinbock L, Elvander M, 2003. Causes of stillbirth and time of death in Swedish Holstein calves examined post mortem. Acta Vet Scand 44(3): 111-120.

Berry DP, Cromie AR, 2009. Associations between age at first calving and subsequent performance in Irish spring calving Holstein-Friesian dairy cows. Livest Sci 123(1): 44-54.

Berry DP, Lee JM, Macdonald KA, Roche JR, 2007. Body condition score and body weight effects on dystocia and stillbirths and consequent effects on postcalving performance. J Dairy Sci 90(9): 4201-4211.

Bicalho RC, Cheong SH, Galvão KN, Warnick LD, Guard CL, 2007. Effect of twin birth calvings on milk production, reproductive performance, and survival of lactating cows. J Am Vet Med Assoc 231: 1390-1397.

Bicalho RC, Galvão KN, Warnick LD, Guard CL, 2008. Stillbirth parturition reduces milk production in Holstein cows. Prev Vet Med 84: 112-120.

Bitaraf Sani M, Amanloo H, 2007. Heat stress effect on open days in Holstein dairy cattle in Yazd province, Iran, 3rd Cong of Animal Science, Mashhad, Iran. p: 85.

Breazile JE, Vollner LA, Rice LE, 1988. Neonatal adaptation to stress of parturition and dystocia. Vet Clin North Am Food Anim Pract 4(3): 481-499.

Bruun J, Ersbøll AK, Alban L, 2002. Risk factors for metritis in Danish dairy cows. Prev Vet Med 54: 179-190.

Buoen LC, Zhang TQ, Wever AF, Ruth GR, 1992. Nonfreemartin rate in Holstein heterosexual twins. Am Assoc Bov Pract Confr 1: 300-303.

Butler WR, 2003. Energy balance relationships with follicular development, ovulation and fertility in postpartum dairy cows. Livest Prod Sci 83: 211-218.

Butler WR, 2005. Inhibition of ovulation in the postpartum cow and the lactating sow. Livest Prod Sci 98: 5-12.

Cady RA, Van Vleck LD, 1978. Factors affecting twinning and effects of twinning in Holstein dairy cattle. J Anim Sci 46(4): 950-956.

Carnier P, Albera A, Dal Zotto R, Groen AF, Bona M, Bittante G, 2000. Genetic parameters for direct and maternal calving ability over parities in Piedmontese cattle. J Anim Sci 78(10): 2532-2539.

Chassagne M, Barnouin J, Chacornac JP, 1999. Risk factors for stillbirth in Holstein heifers under field conditions in France: A prospective survey. Theriogenology 51: 1477-1488.

Chu SY, Kim SY, Lau J, Schmid CH, Dietz PM, Callaghan WM, Curtis KM, 2007. Maternal obesity and risk of stillbirth: a metaanalysis. Am J Obstet Gynecol 197: 223-228.

Civelek T, Celik HA, Avci G, Cingi CC, 2008. Effects of dystocia on plasma cortisol and cholesterol levels in Holstein heifers and their newborn calves. Bull Vet Inst Pulawy 52(4): 649-654.

Coleman DA, Thayne WV, Dailey RA, 1985. Factors affecting reproductive performance of dairy cows. J Dairy Sci 68: 1793-1803.

Correa MT, Erb H, Scarlett J, 1993. Path analysis of seven postpartum disorders of Holstein cows. J Dairy Sci 76: 1305-1312.

Day JD, Weaver LD, Franti CE, 1995. Twin pregnancy diagnosis in Holstein cows: discriminatory powers and accuracy of diagnosis by transrectal palpation and outcome of twin pregnancies. Can Vet J 36: 93-97.

Deluyker HA, Gay JM, Weaver LD, Azairi AS, 1991. Change of milk yield with clinical diseases for a high producing dairy herd. J Dairy Sci 74: 436-445.

Dematawewa CMB, Berger PJ, 1997. Effect of dystocia on yield, fertility, and cow losses and an economic evaluation of dystocia scores for Holsteins. J Dairy Sci 80(4): 754-761.

De Vries A, Overton M, Fetrow J, Leslie K, Eicker S, Rogers G, 2008. Exploring the impact of sexed semen on the structure of the dairy industry. J Dairy Sci 91: 847-856.

De Vries A, Olson JD, Pinedo PJ, 2010. Reproductive risk factors for culling and productive life in large dairy herds in the eastern United States between 2001 and 2006. J Dairy Sci 93(2): 613-623.

Dobson H, Tebble JE, Smith RF, Ward WR, 2001. Is stress really all that important? Theriogenology 55(1): 65-73.

Dobson H, Smith RF, Bell GJC, Leonard DM, Richards B, 2008. (Economic) Costs of difficult calvings (in the UK dairy herd): how vets can alleviate the negative impact. Cattle Pract 16: 80-85.

Dohmen MJW, Joop K, Sturk A, Bols PEJ, Lohuis JACM, 2000. Relationship between intra-uterine bacterial contamination, endotoxin levels and the development of endometritis in postpartum cows with dystocia or retained placenta. Theriogenology 54(7): 1019-1032.

Dubuc J, Duffield TF, Leslie KE, Walton JS, LeBlanc SJ, 2011. Effects of postpartum uterine diseases on milk production and culling in dairy cows. J Dairy Sci 94: 1339-1346.

Dwyer CM, Lawrence AB, Bishop SC, 2001. The effects of selection for lean tissue content on maternal and neonatal lamb behaviours in Scottish Blackface sheep. Anim Sci 72: 555-571.

Eaglen SAE, Bijma P, 2009. Genetic parameters of direct and maternal effects for calving ease in Dutch Holstein-Friesian cattle. J Dairy Sci 92(5): 2229-2237.

Eaglen SAE., Coffey MP, Banos G, Woolliams JA, Wall E, 2010a. Analysis of calving traits and gestation length in UK Holstein heifers using an animal model. Proc 9th World Cong Genet Appl Livest Prod, Leipzig, Germany. Paper ID: 0599.

Eaglen SAE, Woolliams JA, Coffey MP, Wall E, 2010b. Effect of calving ease on the subsequent performance of the cow and calf in UK Holstein-Friesian cattle. Proc Ann Conf Br Soc Anim Sci, Belfast, UK, p: 164.

Eaglen SAE, Woolliams JA, Coffey MP, Wall E, 2011. Genetic correlations between calving ease and fertility traits in UK Holstein Friesian heifers. Proc Ann Conf Br Soc Anim Sci, Nottingham, UK. p: 14.

Echternkamp SE, 1992. Fetal development in cattle with multiple ovulations. J Anim Sci 70: 2309-2321.

Echternkamp SE, Gregory KE, 1999. Effects of twinning on postpartum reproductive performance in cattle selected for twin births. J Anim Sci 77: 48-60.

Echternkamp SE, Thallman RM, Cushman RA, Allan MF, Gregory KE, 2007. Increased calf production in cattle selected for twin ovulations. J Anim Sci 85: 3239-3248.

Elkjær K, Labouriau R, Ancker ML, Gustafsson H, Callesen H, 2013. Large-scale study on effects of metritis on reproduction in Danish Holstein cows. J Dairy Sci 96: 372-377.

Emanuelson U, Oltenacu PA, Gröhn YT, 1993. Nonlinear mixed model analyses of five production disorders of dairy cattle. J Dairy Sci 76: 2765-2772.

Erb HN, Martin SW, Ison N, Swaminathan S, 1981. Interrelationships between production and reproductive diseases in Holstein cows. Path analysis. J Dairy Sci 64: 282-289.

Erb HN, Smith RD, Oltenacu PA, Guard CL, Hillman RB, Powers PA, Smith MC, White ME, 1985. Path model of reproductive disorders and performance, milk fever, mastitis, milk yield, and culling in Holstein cows. J Dairy Sci 68: 3337-3349.

Eriksson S, Nasholm A, Johansson K, Philipsson J, 2004. Genetic parameters for calving difficulty, stillbirth, and birth weight for Hereford and Charolais at first and later parities. J Anim Sci 82(2): 375-383.

Esslemont RJ, Kossaibati MA, 1996. Incidence of production diseases and other health problems in a group of dairy herds in England. Vet Rec 139: 486-490.

Fisher MW, Mellor DJ, 2002. The welfare implications of shepherding during lambing in extensive New Zealand farming systems. Anim Welfare 11(2): 157-170.

Forar AL, Gay JM, Hancock DD, Gay CC, 1996. Fetal loss frequency in ten Holstein dairy herds. Theriogenology 45: 1505-1513.

Fourichon C, Seegers H, Bareille N, Beaudeau F, 1999. Effects of disease on milk production in the dairy cow: a review. Prev Vet Med 41: 1-35.

Fourichon C, Seegers H, Malher X, 2000. Effect of disease on reproduction in the dairy cow: a meta-analysis. Theriogenology 53: 1729-1759.

Fricke PM, 2001. Review: twinning in dairy cattle. Prof Anim Sci 17: 61-67.

Fries R, Ruvinsky A, 1999. The genetics of cattle, 1st ed. CABI Publ, NY. pp: 59-60.

Gaafar HMA, Shamiah ShM, Shitta AA, Ganah HAB, 2010. Factors affecting retention of placenta and its influence on postpartum reproductive performance and milk production in Friesian cows. Slovak J Anim Sci 43(1): 6-12.

Gaafar HMA, Shamiah ShM, Abu El-Hamd MA, Shitta AA, Tag El-Din MA, 2011. Dystocia in Friesian cows and its effects on postpartum reproductive performance and milk production. Trop Anim Health Prod 43: 229-234.

Geoffrey HA, Noakes DE, Pearson H, Parkinson TJ, 1992. Veterinary reproduction and obstetrics, 6th ed. Saunders Publ.

Ghavi Hossein-Zadeh N, 2010a. Evaluation of the effect of twin births on the perinatal calf mortality and productive performance of Holstein dairy cows. Arch Tierz 53: 256-265.

Ghavi Hossein-Zadeh N, 2010b. The effect of twinning on milk yield, dystocia, calf birth weight and open days in

Holstein dairy cows of Iran. J Anim Physiol Anim Nutr 94: 780-787.

Ghavi Hossein-Zadeh N, 2011. Estimation of genetic parameters and genetic change for stillbirth in Iranian Holstein cows: a comparison between linear and threshold models. Agric Food Sci 20: 287-297.

Ghavi Hossein-Zadeh N, 2013. Study on the effect of dystocia on the productive performance and calf stillbirth in Iranian Holsteins. J Agric Sci Technol. [In press].

Ghavi Hossein-Zadeh N, Ardalan M, 2011a. Evaluation of the potential effects of abortion on the productive performance of Iranian Holstein dairy cows. Anim Sci J 82: 117-121.

Ghavi Hossein-Zadeh N, Ardalan M, 2011b. Bayesian estimates of genetic parameters for metritis, retained placenta, milk fever, and clinical mastitis in Holstein dairy cows via Gibbs sampling. Res Vet Sci 90: 146-149.

Ghavi Hossein-Zadeh N, Ardalan M, 2011c. Cow-specific risk factors for retained placenta, metritis and clinical mastitis in Holstein cows. Vet Res Com 35: 345-354.

Ghavi Hossein-Zadeh N, Nejati-Javaremi A, Miraei-Ashtiani SR, Kohram H, 2008. An observational analysis of twin births, calf stillbirth, calf sex ratio, and abortion in Iranian Holsteins. J Dairy Sci 91: 4198-4205.

Ghavi Hossein-Zadeh N, Nejati-Javaremi A, Miraei-Ashtiani SR, Kohram H, 2009. Estimation of variance components and genetic trends for twinning rate in Holstein dairy cattle of Iran. J Dairy Sci 92: 3411-3421.

Ghavi Hossein-Zadeh N, Nejati-Javaremi A, Miraei-Ashtiani SR, Kohram H, 2010. Bioeconomic evaluation of the use of sexed semen at different conception rates and herd sizes in Holstein populations. Anim Reprod Sci 121: 17-23.

Ghavi Hossein-Zadeh N, Nejati-Javaremi A, Miraei-Ashtiani SR, Kohram H, Honarvar M, 2011. Bio-economic model to evaluate twinning rate using sexed embryo transfer in dairy herds. Animal 5: 1705-1719.

Ghorbani G, Asadi-Alamoti A, 2004. Developed management of dairy cattle, 1st ed. Industrial Unit of Jahad, Isfahan, Iran. 260 pp.

Goff JP, 2006. Major advances in our understanding of nutritional influences on bovine health. J Dairy Sci 89: 1292-1301.

Goff JP, Horst RL, 1997. Physiological changes at parturition and their relationship to metabolic disorders. J Dairy Sci 80: 1260-1268.

Goonewardene LA, Wang Z, Price MA, Yang R-C, Berg RT, Makarechian M, 2003. Effect of udder type and calving assistance on weaning traits of beef and dairy × beef calves. Livest Prod Sci 81(1): 47-56.

Goshen T, Shpigel NY, 2006. Evaluation of intrauterine antibiotic treatment of clinical metritis and retained fetal membranes in dairy cows. Theriogenology 66: 2210-2218.

Grimard B, Freret S, Chevallier A, Pinto A, Ponsart C, Humblot P, 2006. Genetic and environmental factors influencing first service conception rate and late embryonic/foetal mortality in low fertility dairy herds. Anim Reprod Sci 91(1-2): 31-44.

Gröhn YT, Rajala-Schultz PJ, 2000. Epidemiology of reproductive performance in dairy cows. Anim Reprod Sci 60/61: 605-614.

Gröhn YT, Erb HN, McCulloch CE, Saloniemi HS, 1990. Epidemiology of mammary gland disorders in multiparous Finnish Ayrshire cows. Prev Vet Med 8: 241-252.

Gröhn YT, Rajala-Schultz PJ, Allore HG, DeLorenzo MA, Hertl JA, Galligan DT, 2003. Optimizing replacement of dairy cows: modeling the effects of diseases. Prev Vet Med 61: 27-43.

Grummer RR, Mashek DG, HayIrli A, 2004. Dry matter intake and energy balance in the transition period. Vet Clin N Am-Food Anim Pract 20: 447-470.

Guerra-Martinez P, Dickerson GE, Anderson GB, Green RD, 1990. Embryo-transfer, twinning and performance efficiency in beef production. J Anim Sci 68: 4039-4050.

Gundelach Y, Essmeyer K, Teltscher MK, Hoedemaker M, 2009. Risk factors for perinatal mortality in dairy cattle: cow and foetal factors, calving process. Theriogenology 71(6): 901-909.

Han IK, Kim IH, 2005. Risk factors for retained placenta and the effect of retained placenta on the occurrence of postpartum diseases and subsequent reproductive performance in dairy cows. J Vet Sci 6: 53-59.

Hansen PJ, 2002. Embryonic mortality in cattle from the embryo's prospective. J Anim Sci 80 (Suppl. 2): E33-E44.

Hansen M, Misztal I, Lund MS, Pedersen J, Christensen LG, 2004. Undesired phenotypic and genetic trend for stillbirth in Danish Holsteins. J Dairy Sci 87: 1477-1486.

Hanson T, Bedrick EJ, Johnson WO, Thurmond MC, 2003. A mixture model for bovine abortion and foetal survival. Stat Med 22: 1725-1739.

Heinrichs AJ, Heinrichs BS, 2011. A prospective study of calf factors affecting first-lactation and lifetime milk production and age of cows when removed from the herd. J Dairy Sci 94(1): 336-341.

Heins BJ, Hansen LB, Seykora AJ, 2006. Calving difficulty and stillbirths of pure Holsteins *versus* crossbreds of Holstein with Normande, Montbeliarde, and Scandinavian Red. J Dairy Sci 89: 2805-2810.

Henderson L, Miglior F, Sewalem A, Kelton D, Robinson A, Leslie KE, 2011. Estimation of genetic parameters for measures of calf survival in a population of Holstein heifer calves from a heifer-raising facility in New York State. J Dairy Sci 94(1): 461-470.

Hickson RE, Morris ST, Kenyon PR, López-Villalobos N, 2006. Dystocia in beef heifers: a review of genetic and nutritional influences. N Z Vet J 54(6): 256-264.

Hovingh E, 2009. Abortions in dairy cattle: I. Common causes of abortions. Virginia Coop. Ext Publ 404-288. Virginia Polytechn Inst and State Univ, Blacksburg.

Hur TY, Jung YH, Kang SJ, Choe CY, Kim UH, Ryu IS, Son DS, Park SJ, Kim IH, 2011. The impact of the duration of retained placenta on postpartum diseases and culling rates in dairy cows. Korean J Vet Res 51(3): 233-237.

Huzzey JM, Veira DM, Weary DM, von Keyserlingk MAG, 2007. Prepartum behavior and dry matter intake identify dairy cows at risk for metritis. J Dairy Sci 90: 3220-3233.

Jamaluddin AA, Case JT, Hird DW, Blanchard PC, Peauroi JR, Anderson ML, 1996. Dairy cattle abortion in California: evaluation of diagnostic laboratory data. J Vet Diagn Invest 8: 210-218.
Johanson JM, Berger PJ, 2003. Birth weight as a predictor of calving ease and perinatal mortality in Holstein cattle. J Dairy Sci 86(11): 3745-3755.
Kaneene JB, Miller R, 1995. Risk factors for metritis in Michigan dairy cattle using herd- and cow-based modelling approaches. Prev Vet Med 23: 183-200.
Kaneko K, Kawakami S, Miyoshi M, Abukawa T, Yamanka S, Mochizuki M, Yoshihara S, 1997. Effect of retained placenta on subsequent bacteriological and cytological intrauterine environment and reproduction in Holstein dairy cows. Theriogenology 48: 617-624.
Khodakaram-Tafti A, Ikede BO, 2005. A retrospective study of sporadic bovine abortions, stillbirths, and neonatal abnormalities in Atlantic Canada, from 1990 to 2001. Can Vet J 46: 635-637.
Kirkpatrick BW, 2002. Management of twinning cow herds. J Anim Sci 80(E. Suppl 2): E14-E18.
Komisarek J, Dorynek Z, 2002. Genetic aspects of twinning in cattle. J Appl Genet 43(1): 55-68.
Könyves L, Szenci O, JurkovichV, Tegzes L, Tirián A, Solymosi N, Gyulay G, Brydl E, 2009. Risk assessment and consequences of retained placenta for uterine health, reproduction and milk yield in dairy cows. Acta Vet Brno 78: 163-172.
Kossaibati MA, Esslemont RJ, 1997. The costs of production diseases in dairy herds in England. Vet J 154: 41-51.
Labernia J, López-Gatius F, Santolaria P, Lopez-Bejar M, Rutllant J, 1996. Influence of management factors on pregnancy attrition in dairy cattle. Theriogenology 45: 1247-1253.
Laven RA, Peters AR, 1996. Bovine retained placenta: aetiology, pathogenesis and economic loss. Vet Rec 139: 465-471.
LeBlanc SJ, 2008. Postpartum uterine disease and dairy herd reproductive performance: a review. Vet J 176: 102-114.
Le Cozler Y, Lollivier V, Lacasse P, Disenhaus C, 2008. Rearing strategy and optimizing first-calving targets in dairy heifers: a review. Animal 2(9): 1393-1404.
Lee J, Hwa Kim I, 2007. Pregnancy loss in dairy cows: the contributing factors, effect on reproductive performance and the economic impact. J Vet Sci 8(3): 283-288.
Lombard JE, Garry FB, Tomlinson SM, Garber LP, 2007. Impacts of dystocia on health and survival of dairy calves. J Dairy Sci 90(4): 1751-1760.
López de Maturana E, Legarra A, Varona L, Ugarte E, 2007a. Analysis of fertility and dystocia in Holsteins using recursive models to handle censored and categorical data. J Dairy Sci 90(4):2012-2024.
López de Maturana E, Ugarte E, González-Recio O, 2007b. Impact of calving ease on functional longevity and herd amortization costs in Basque Holsteins using survival analysis. J Dairy Sci 90(9): 4451-4457.
López-Gatius F, Hunter RHF, 2005. Spontaneous reduction of advanced twin embryos: its occurrence and clinical relevance in dairy cattle. Theriogenology 63: 118-125.
López-Gatius F, 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. Reprod Domest Anim 45(S 3): 15-24.
López-Gatius F, Santolaria P, Yániz J, Rutllant J, López-Béjar M, 2002. Factors affecting pregnancy loss from gestation day 38 to 90 in lactating dairy cows from a single herd. Theriogenology 57: 1251-1261.
López-Gatius F, Szenci O, Bech-Sàbat G, García-Ispierto I, Serrano B, Santolaria P, Yániz J, 2009. Factors of non-infectious nature affecting late embryonic and early foetal loss in high producing dairy herds in north-eastern Spain. Magyar Allatorvosok Lapja 131: 515-531.
Lucey S, Rowlands GJ, Russell A, 1986. Short-term associations between disease and milk yield of dairy cows. J Dairy Res 53: 7-15.
Maizon DO, Oltenacu PA, Gröhn YT, Strawderman RL, Emanuelson U, 2004. Effects of diseases on reproductive performance in Swedish Red and White dairy cattle. Prev Vet Med 66: 113-126.
Mangurkar BR, Hayes JF, Moxley JE, 1984. Effects of calving ease-calf survival on production and reproduction in Holsteins. J Dairy Sci 67: 1496-1509.
Markusfeld O, 1984. Factors responsible for post parturient metritis in dairy cattle. Vet Rec 114: 539-542.
Markusfeld O, 1986. The association of displaced abomasums with various pariparturient factors in dairy cows. A retrospective study. Prev Vet Med 4: 173-183.
Markusfeld O, 1987. Periparturient traits in seven high dairy herds. Incidence rates, association with parity, and interrelationships among traits. J Dairy Sci 70: 158-166.
Markusfeld-Nir O, 1997. Epidemiology of bovine abortions in Israeli dairy herds. Prev Vet Med 31: 245-255.
Martin JM, Wilcox CJ, Moya J, Klebanow EW, 1986. Effects of retained fetal membranes on milk yield and reproductive performance. J Dairy Sci 69: 1166-1168.
McGuirk BJ, Forsyth R, Dobson H, 2007. Economic cost of difficult calvings in the United Kingdom dairy herd. Vet Rec 161(20): 685-687.
Mee JF, 1991. Perinatal calf mortality-recent findings. Irish Vet J 44: 80-83.
Mee JF, 2004. Managing the dairy cow at calving time. Vet Clin North Am Food Anim Pract 20(3): 521-546.
Mee JF, 2008a. Prevalence and risk factors for dystocia in dairy cattle: a review. Vet J 176(1): 93-101.
Mee JF, 2008b. Newborn dairy calf management. Vet Clin North Am Food Anim Pract 24(1): 1-17.
Mee JF, 2008c. Perinatal mortality in heifers – An emerging problem. Cattle Pract 16: 166-173.
Mee JF, 2010. A clinical and pathological investigation of perinatal mortality in dairy calves: preliminary results from a recent prospective study. Proc Br Soc Anim Sci, Belfast, UK. p: 156.
Meijering A, 1984. Dystocia and stillbirth in cattle – A review of causes, relations and implications. Livest Prod Sci 11(2): 143-177.
Meléndez P, McHale J, Bartolome J, Archbald LF, Donovan GA, 2004. Uterine involution and fertility of Hols-

tein cows subsequent to early postpartum PGF2 alpha treatment for acute puerperal metritis. J Dairy Sci 87: 3238-3246.

Meyer CL, Berger PJ, Koehler KJ, Thompson JR, Sattler CG, 2000. Interactions among factors affecting stillbirths in Holstein Cattle in the United States. J Dairy Sci 83: 2657-2663.

Meyer CL, Berger PJ, Koehler KJ, Thompson JR, Sattler CG, 2001. Phenotypic trends in incidence of stillbirth for Holsteins in the United States. J Dairy Sci 84(2): 515-523.

Muller LD, Owens MJ, 1974. Factors associated with the incidence of retained placentas. J Dairy Sci 57: 725-728.

Nakao T, Grunert E, 1990. Effects of dystocia on postpartum adrenocortical function in dairy cows. J Dairy Sci 73(10): 2801-2806.

Nielen M, Schukken YH, Scholl DT, Wilbrink HJ, Brand A, 1989. Twinning in dairy cattle: a study of risk factors and effects. Theriogenology 32: 845-862.

Opsomer G, Grohn YT, Hertl J, Coryn M, Deluyker H, 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.

Østergaard S, Gröhn YT, 1999. Effects of diseases on test day milk yield and body weight of dairy cows from Danish research herds. J Dairy Sci 82: 1188-1201.

Ouweltjes W, Smolders EAA, Elving L, Van Eldik P, Schukken YH, 1996. Fertility disorders and subsequent fertility in dairy cattle. Livest Prod Sci 46: 213-220.

Overton M, Fetrow J, 2008. Economics of postpartum uterine health. Proc of Dairy Cattle Reproduction Council Convention. Omaha, NE, USA. pp: 39-43.

Peter AT, 2000. Abortions in dairy cows: New insights and economic impact. Adv Dairy Technol 12: 233-244.

Philipsson J, 1976a. Calving performance and calf mortality. Livest Prod Sci 3(4): 319-331.

Philipsson J, 1976b. Studies on calving difficulty, stillbirth and associated factors in Swedish cattle breeds. IV. Relationships between calving performance, precalving body measurements and size of pelvic opening in Friesian heifers. Acta Vet Scand 26(3): 221-229 (abstr.).

Philipsson J, Foulley JL, Lederer J, Liboriussen T, Osinga A, 1979. Sire evaluation standards and breeding strategies for limiting dystocia and stillbirth. Report of an EEC/EAAP working group. Livest Prod Sci 6: 111-127.

Proudfoot KL, Huzzey JM, Von Keyserlingk MAG, 2009. The effect of dystocia on the dry matter intake and behavior of Holstein cows. J Dairy Sci 92(10): 4937-4944.

Rafati N, Mehrabani-Yeganeh, Hansonb TE, 2010. Risk factors for abortion in dairy cows from commercial Holstein dairy herds in the Tehran region. Prev Vet Med 96: 170-178.

Rajala PJ, Gröhn YT, 1998. Effects of dystocia, retained placenta, and metritis on milk yield in dairy cows. J Dairy Sci 81(12): 3172-3181.

Riley DG, Chase Jr CC, Olson TA, Coleman SW, Hammond AC, 2004. Genetic and nongenetic influences on vigor at birth and preweaning mortality of purebred and high percentage Brahman calves. J Anim Sci 82(6): 1581-1588.

Rossoni A, Nicoletti C, Ghiroldi S, Santus E, Bagnato A, 2005. Calf's suckling ability in Italian Brown Swiss. Interbull Bull 33: 218-221.

Rowlands GJ, Lucey S, 1986. Changes in milk yield in dairy cows associated with metabolic and reproductive disease and lameness. Prev Vet Med 4: 205-221.

Roxstrom A, Strandberg E, Berglund B, Emanuelson U, Philipsson J, 2001. Genetic and environmental correlations among female fertility traits and milk production in different parities of Swedish red and white dairy cattle. Acta Agric Scand A Anim Sci 51: 7-14.

Santos JEP, Juchem SO, Galvao KN, Cerri RLA, 2003. Transition cow management to reduce metabolic diseases and improve reproductive management. Adv Dairy Technol 15: 287-305.

Senger PL, 2003. Pathways to pregnancy and parturition, 2nd ed (Senger PL, ed). Cadmus Prof Comm, Ephrata, PA, USA.

Sheldon IM, Lewis GS, LeBlanc S, Gilbert RO, 2006. Defining postpartum uterine disease in cattle. Theriogenology 65: 1516-1530.

Silva del Río N, Stewart S, Rapnicki P, Chang YM, Fricke PM, 2007. An observational analysis of twin births, calf sex ratio, and calf mortality in Holstein dairy cattle. J Dairy Sci 90: 1255-1264.

Simerl NA, Wilcox CJ, Thatcher WW, 1992. Postpartum performance of dairy heifers freshening at young ages. J Dairy Sci 75: 590-595.

Sorge US, Kelton DF, Staufenbiel R, 2008. Short communication: Prepartal concentration of estradiol-17 beta in heifers with stillborn calves. J Dairy Sci 91(4): 1433-1437.

Steenholdt C, Hernández J, 2004. Risk factors for umbilical hernia in Holstein heifers during the first two months after birth. J Am Vet Med Assoc 224(9): 1487-1490.

Steinbock L, Näsholm A, Berglund B, Johansson K, Philipsson J, 2003. Genetic effects on stillbirth and calving difficulty in Swedish Holsteins at first and second calving. J Dairy Sci 86(6): 2228-2235.

Stevenson JS, Call EP, 1988. Reproductive disorders in the periparturient dairy cow. J Dairy Sci 71: 2572-2583.

Tenhagen BA, Helmbold A, Heuwieser W, 2007. Effect of various degrees of dystocia in dairy cattle on calf viability, milk production, fertility and culling. J Vet Med A Physiol Pathol Clin Med 54: 98-102.

Thompson JR, Pollak EJ, Pelissier CL, 1983. Interrelationships of parturition problems, production of subsequent lactation, reproduction, and age at first calving. J Dairy Sci 66(5): 1119-1127.

Thurmond MC, Picanso JP, Jameson CM, 1990. Considerations for use of descriptive epidemiology to investigate fetal loss in dairy cows. J Amer Vet Med Assoc 197: 1305-1312.

Thurmond MC, Branscum AJ, Johnson WO, Bedrick EJ, Hanson TE, 2005. Predicting the probability of abortion in dairy cows: a hierarchical Bayesian logistic-survival model using sequential pregnancy data. Prev Vet Med 68: 223-239.

Van Werven T, Schukken YH, Lloyd J, Brand A, Heeringa HT, Shea M, 1992. The effect of duration of retained placenta on reproduction, milk production, popartum disease and culling rate. Theriogenlogy 37: 1191-1203.
Vinuela-Fernández I, Jones E, Welsh EM, Fleetwood-Walker SM, 2007. Pain mechanisms and their implication for the management of pain in farm and companion animals. Vet J 174(2): 227-239.
Wiltbank MC, Fricke PM, Sangsritavong S, Sartori R, Ginther OJ, 2000. Mechanisms that prevent and produce double ovulations in dairy cattle. J Dairy Sci 83: 2998-3007.
Wittrock JM, Proudfoot KL, Weary DM, von Keyserlingk MAG, 2009. Metritis causes long term decreases in the milk production of multiparous Holstein dairy cows. Proc 44th Annual Pacific Northwestern Animal Nutrition Conf. Boise, ID, USA. p: 190.
Wittrock JM, Proudfoot KL, Weary DM, Von Keyserlingk MAG, 2011. Metritis affects long-term milk production and cull rate of Holstein dairy cows. J Dairy Sci 94: 2408-2412.
Zaborski D, Grzesiak W, Szatkowska I, Dybus A, Muszynska M, Jedrzejczak M, 2009. Factors affecting dystocia in cattle. Reprod Domest Anim 44: 540-551.