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### ABSTRACT

The perinatal period is the most hazardous in the life of all animals. More than 60% of producers have reported that most of their calf mortality occurs at birth. Calf mortality represents economic losses to the dairy industry due to delayed genetic progress, fewer replacements available for voluntary culling of the lactating herd, and increased cost of replacement. The main causes of perinatal morbidity and mortality are, in descending order of importance, combined respiratory and metabolic acidosis, parturient trauma, hypoglobulinemia, congenital infections and deficiencies, and omphalophlebitis. This indicates that farmers and their veterinarians need to focus on calving management when investigating such problems and when attempting to reduce losses in herds with high rates of bovine perinatal mortality. This paper discusses both the risk factors for, and the ultimate causes of, perinatal mortality and their effects on perinatal calf welfare, an underdocumented topic.

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### INTRODUCTION

Birth and the first hours of life are critical for the subsequent health and survival of calves. Calf survival is influenced by many factors, including genetic, management and environmental variables (Meyer *et al.*, 2001). The perinatal period is the most hazardous in the life of all animals. More than 60% of producers have reported that most of their calf mortality occurs at birth. Perinatal mortality may be defined as death of the perinate prior to, during or within 48 hours of calving, following a gestation period of at least 260 days, irrespective of the cause of death or the circumstances related to calving. The perinatal period is the most hazardous in the life of all animals. Approximately 75% of perinatal mortality occurs within one hour of calving with the remainder occurring either pre- (10%) or post-partum (15%). Some 90% of calves, which die in the perinatal period, were alive at the start of calving and so much of this loss is a preventable welfare problem (Mee, 2008). So many calves die because their death is not prioritized, not only as an economical but also as a welfare problem (Mee, 2013a).

#### **Economical Importance of Perinatal Calf Mortality**

Perinatal mortality has a detrimental effect on cow health, survival, reproductive performance and milk production. In the USA it has been estimated that the economic costs of stillborn calves reach about 125 million US\$ annually due to direct loss of calves. Additional economic losses result from a decreased milk yield and a higher risk of metritis/endometritis and retained placental membranes (Berglund *et al.*, 2009; Steinbock *et al.*, 2003; Bicalho *et al.*, 2007) in the affected dams.

#### **Incidence of Perinatal Calf Mortality**

Several studies reported a continuous increase in the frequency of stillbirth throughout the last decades in many countries (Berglund *et al.*, 2009; Bicalho *et al.*, 2007; Bicalho *et al.*, 2008; Mee *et al.*, 2011). The average incidence of perinatal mortality in cows and heifers varies between 2 and 20% across dairy industries internationally with the



majority of countries between 5 and 8% (Mee, 2008). The variation between national agricultural statistical data averages reflects differences in definitions of perinatal mortality but, more importantly, emphasises the differences between those countries which have practised a long-term policy of genetic selection against undesirable functional traits (e.g., Norway and Sweden) and those which have pursued single trait selection policies (e.g., Canada and the USA) and associated dairy breed differences (Heins *et al.*, 2006).

### **Risk Factors For Perinatal Calf Mortality**

The majority of perinatal mortality has been attributed directly to difficult calving particularly in heifers, which frequently require assistance at calving. Parity has been shown to be the best predictor variable for perinatal mortality followed in heifers by difficult calving and in older cows by difficult calving and gestation length (Mever et al., 2000). Other significant animal-level factors, also common to difficult calving, include age at first calving, particularly in heifers less than 24 months old (Benjaminsson, 2007), twinning (Silva del Rio et al., 2007), foetal gender (Steinbock et al., 2003), shorter or longer gestation length (Meyer et al., 2000) and sire predicted transmitting ability (PTA) for perinatal mortality (Mee, 2008). In recent years, the interplay between genotypic and environmental risk factors has received more scientific attention with the identification of modifiable and non-modifiable risk factors for perinatal mortality (Mee et al., 2013b). Significant herd-level risk factors for perinatal mortality include herd, year, season of calving, larger (>20 cows) herd size and calving management (Mee et al., 2013a). While deficiencies of micro-nutrients (iodine, selenium, copper and zinc) have been associated with high stillbirth rates, results from randomised clinical trials have not always supported a causal relationship (Mee, 1999). Excess body condition prior to calving, particularly in heifers, has been associated with reduced appetite as calving approaches with resultant mobilisation of fat reserves; also it may reduce magnesium availability, and the ensuing sub-clinical hypocalcaemia could produce uterine atony which is observed clinically as 'slow calving syndrome' where foetal death occurs in the absence of difficult calving (non-visible dystocia) (Chassagne et al., 1999). Gundelach et al., (2009) stated that the course of the calving process, especially the duration of the second stage seems to be crucial. The latter can be used to evaluate the course of calving and to ensure timely obstetrical interventions which should be taken into account when second stage of calving lasts longer than 2 h, regardless of parity.

## Age and Parity at Parturition

The risk of perinatal mortality is greater in primiparous cattle compared to multiparous cattle (Mee *et al.*, 2014). In primiparous cattle, a younger age of calving is associated with an increased risk of perinatal mortality (Mee *et al.*, 2014), with the highest risk seen in cattle calving at less than 24 months old, due to inadequate pelvic size (Mee *et al.*, 2014). With calving at the age of 22 months for the first time, the probability of stillbirth for male and female calves is 0.29 and 0.21, respectively, whereas, at an age at first calving of 28 months, the corresponding values were 0.15 and 0.10 (Hansen *et al.*, 2004).

### Gender of Calf

The sex of the calf is thought to play a role in the incidence of perinatal mortality, with almost twice as many male losses compared to female losses (Meijering, 1984). Male calves tend to have longer gestations (over one day) than female calves (Mee, 2011) and this increases risks of dystocia and perinatal losses. Where perinatal mortality occurs following a normal parturition, there is very little difference between genders of calves (Meijering, 1984; Norquay, 2017).

### Weight of Calf

It has been estimated that greatest predictor of dystocia risk is calf birth weight (Mee & Szenci, 2012) and the frequency of dystocia rises when the weight of the calf reaches a certain threshold (Meijering, 1984). The weight of the calf has been discussed in the nutrition section above. Male calves have a 9% greater birth weight compared to female calves Differences in weight between genders are relatively constant across breeds (Holland and Odde, 1992). In large calves, dystocia may result in anoxia and metabolic and respiratory acidosis, which may lead to reduced immunoglobulin absorption and increased disease susceptibility (Norquay, 2017; Holland and Odde, 1992).

### **Causes of Perinatal Calf Mortality**

The major causes of bovine perinatal mortality as described in recent necropsy studies internationally are dystocia (approximately 35%) and anoxia (approximately 30%), to a much lesser extent, other causes (approximately 15%), infections (approximately 5%) and congenital defects (approximately 5%). On average, some 25% of cases have no diagnosed cause but this varies between approximately 5% and 50% between studies.

## Dystocia

Up to one-third of dairy calves are born after dystocia (calving difficulty requiring assistance at birth) and this is a major cause of calf mortality. There is a strong association between stillbirths and calving difficulty (Berglund *et al.*, 2009), although it is often difficult to determine the exact timing of calf death. In cattle, dystocia is a major factor contributing to perinatal mortality (Meyer *et al.*, 2001; Berglund *et al.*, 2009). The primary causes of dystocia in primiparea cows are relative foetal oversize and in pluriparae maldispositions (Mee, 2018). Internationally, the incidence of severe dystocia in dairy cattle ranges from 2% to 22%, while the proportion of assisted calvings is higher, ranging from 10% to 50% (2). Risk factors for calving difficulty include breed, sire, parity, gestation length, calf sex, twinning, season of birth, herd size and calving supervision (Svensson *et al.*, 2006). Traumatic lesions found in stillborn calves associated with dystocia include fractured and dislocated ribs, fractured spine, fractured legs, fractured mandible, diaphragmatic tears or hernia, hepatic rupture (Figure 1), renal haematoma, subcutaneous haemorrhages, bruising or oedema around the neck, subdural haemorrhages, internal haemorrhage, and collapsed trachea (Mee *et al.*, 2013b). The most common lesions recorded are fractures of the ribs or the spine. The trauma associated with dystocic mortality is clearly a serious animal welfare issue arising from the pain and suffering the calf endures.



Figure 1. Hepatic rupture caused by trauma during difficult calving assistance.

### Infections

Unlike abortions where infections constitute the major proportion of diagnosed causes, in perinatal mortality infections are a minor diagnosed cause varying between 3% and 15% between published studies. In a recent study of Polish dairy herds, Jawor et al 2017 (Jawor *et al.*, 2017) showed that 14.9% of calves showed evidence of exposure to infection (antibody-positive). The most common infections, in descending order, were parasitic, viral and bacterial.

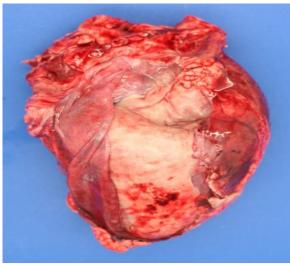


Figure 2. Extensive fibrinous pericarditis in a stillborn calf

The infectious agents associated with abortion are the same ones associated with perinatal mortality; Truperella pyogenes, Bacillus spp, bovine viral diarrhoea virus, Brucella abortus, Coxiella burnetii, fungi, Leptospira hardjo, Neospora caninum, Pasteurella multocida and Salmonella dublin. In addition, inflammatory lesions indicative of bacterial infection [(e.g., bronchopneumonia, encephalitis, pericarditis (Fig 2)] are used as diagnostic criteria for

infection as a cause of death in cases of perinatal mortality and are often ranked as the most commonly detected criterion. In utero mortality caused by pathogenic infections do not compromise animal welfare, however, the death of perinates born following in utero, transvaginal or postnatal infections which subsequently suffer from the consequent inflammatory lesions, e.g., omphalophlebitis, pleuro-pneumonia, peritonitis, is an animal welfare issue (Norquay, 2017; Jawor *et al.*, 2017; Anderson, 2007; Mee, 2013b).

### Anoxia

Anoxia (absence of oxygen reaching the tissues) and hypoxia result from impaired oxygen delivery to cells and decreased tissue perfusion. Both may affect cardiac function (Aydogdu et al., 2016). Both are often a sequel to dystocia; however, premature placental separation, foetal stress and umbilical occlusion resulting from prolonged parturition may also be a cause (Mee, 1999). Neonatal hypoxic ischaemia usually leads to cardiovascular disorders. Oxygen depletion due to secondary hypoxic ischaemia is thought to cause myocardial injury (Sweetman et al., 2012). Premature calves have surfactant deficiency (Divers, 2008). Insufficient surfactant leads to end-expiratory collapse of lung regions that are inadequately, or not at all, aerated. These atelectatic regions result in inadequate surface area for gas exchange, and the neonate increases its respiratory rate to maintain adequate ventilation. If this is not achieved, hypoxia ensues (Bleul, 2009). Preterm and term calves with foetal and Neonatal respiratory distress syndrome have high mortality because of hypoxia, hypercapnia, and acidosis (Szenci et al., 1989). Anoxic lesions, often found following clinical dystocia and 'non-clinical dystocia' (clinically undetectable prolonged or abnormal stage one or two of calving), include pulmonary atelectasis, subserosal haemorrhages (pleural, tracheal, scleral, epicardial, endocardial), organ congestion (liver, kidneys, conjunctiva, meninges), meconium aspiration syndrome (MAS) and meconium staining or passage (Mee, 2008; Mee, 2013b). Unfortunately, calves dying following acute anoxia often have unremarkable gross pathological findings. Prolonged hypoxia may cause more pronounced lesions (Norquay, 2017; Mee, 2014). Mortality due to acute anoxia where the foetus has not achieved a conscious state is not an animal welfare issue. Even though chronic hypoxia may result in pronounced physiochemical stress and grossly visible extensive lesions upon necropsy, if the foetus is not conscious during these life-threatening changes, technically this does not impact upon its welfare.

### **Congenital Defects**

Congenital defects may be defined as any defect in the foetus present at birth. The cause of many congenital defects is unknown, but some are inherited. Congenital defects can also occur as a result of genetic mutation, exposure to infectious agents, pharmaceutical teratogens and toxins (Whitlock *et al.*, 2008). The cause of some deaths will be obvious, others will be much more difficult to diagnose. Anatomical abnormalities are those most commonly diagnosed by veterinary practitioners and non-specialist veterinary diagnostic laboratories (Norquay, 2017). The incidence and types of congenital defects are highly variable depending primarily on the survey methodology. Hence, the number and types of cases submitted to veterinary institutions (research labs, routine diagnostic labs, and veterinary faculties) may differ greatly from those actually occurring on farms, and observed by veterinary practitioners, which are not submitted. This submission bias may result in fewer but more severe cases being submitted than non-submitted. In cases of perinatal mortality, congenital defects seen include intestinal atresia, arthrogryposis, cerebellar hypoplasia, cleft palate, omphalocoele, ventricular septal defect, schistosomus reflexus (Fig 3) and hydrocephalus, which can be readily detected at post-mortem examination (Mee, 2013b).



Figure 3. Congenital defect in a stillborn calf

### Omphalorrhagia

Omphalorrhagia may be defined as bleeding from one or both umbilical arteries. With internal omphalorrhagia the arteries retract into the abdomen but do not constrict completely. The prevalence of omphalorrhagia as a cause of

perinatal mortality is unknown (Mee, 2013b). The severity of cases can range from a small amount of perivascular haemorrhage surrounding the umbilical vessels to extensive haemoperitoneum with no other source of haemorrhage (Mee, 2013b). Severe cases predominantly occur in full term bovine foetuses though they have been recorded in aborted foetuses. Affected calves tend to die between 1 and 48 hours after birth. Such calves are generally found dead without premonitory clinical signs. The most common presenting sign is conjunctival pallor. Farmer treatment of affected cases by ligating the cord is ineffectual as the bleeding is internal. Veterinary practitioners have used blood transfusions and surgical ligation with variable success. The welfare of calves affected by omphalorrhagia is clearly compromised, as they tend to survive for hours or days while continuing to haemorrhage internally and become more anaemic (Norquay, 2017).

### **Premature Placental Separation (PPS)**

In the cow the foetal membranes are normally expelled between 30 minutes and 8 hours after stage two of calving. While premature placental separation (PPS) is a well-recognised condition in the mare, there is a paucity of literature on the condition in cattle. Premature placental separation has been associated with 'weak calf syndrome' in heifers (Mee *et al.*, 2014). It has been associated with premature birth (Aydogdu *et al.*, 2016) and maldisposition (Mee, 2008). Anecdotally, pharmacological induction of parturition, excessive selenium supplementation and subclinical hypocalcaemia have also been implicated. It is considered, where recorded, as a minor cause of perinatal mortality. Calves, which die following PPS do so due to anoxia or haemorrhage in utero or during calving and as such their welfare is not compromised.

To aid in perinatal mortality investigation, placental tissue should be examined when available (Anderson, 2007). In many situations, the placenta is unavailable for examination due to delayed expulsion of the placenta after delivery of the calf. In fresh placental tissue, red cotyledons are present with a clear, translucent inter-cotyledonary area (Anderson, 2007). When autolysis is present, the intercotyledonary placenta becomes less translucent and the cotyledons change to dull brown (Anderson, 2007). Inflammation in the chorio-allantois can be seen by opacity in the inter-cotyledonary area, thickening or exudate on the surface and depression of the cotyledons relative to the surrounding inter-cotyledonary area (Anderson, 2007).

## **Trace Element Disorders**

Trace mineral and vitamin deficiencies contribute to a number of causes of foetal, neonatal, and postnatal losses in beef calves (Waldner & Blakley, 2014), with the maternal micronutrient status being the primary determinant of micronutrient status in the neonate (Mee, 2013b). Classical deficiency of trace elements, for example iodine (Mee, 2008) and selenium (Mee, 2013b), is still associated with high perinatal mortality rates in individual herds, particularly in heifers. Associations have also been made between herd blood copper, zinc and selenium status and perinatal mortality (Norquay, 2017). Thyroid insufficiency is typically seen clinically as calves born with goitres, but other clinical signs may also be seen, including poor hair quality, foetal death (including abortions and stillbirths), and the birth of premature or weak calves with low birth weights (Cutler & Jones, 2003). There are three main recognized causes of thyroid insufficiency; iodine deficiency, goitrogens and selenium deficiency. Respiratory distress syndrome (RDS) in calves has conventionally been associated with prematurity. However, recent research indicates that RDS in mature Belgian Blue calves may be associated with trace element deficiency-induced surfactant insufficiency; specifically, deficiencies of selenium, copper, zinc and iodine (Mee, 1994). The proportion of perinatal mortality attributable to iodine imbalance is variable in published studies reflecting differences in animal husbandry and diagnostic criteria. Trace element deficiency-induced RDS directly impacts animal welfare as such calves survive after calving but have great difficulty in breathing and, even if diagnosed and treated, many die (Mee, 1999).

## CONCLUSIONS

High bovine perinatal mortality rates remain an international welfare problem though this is often not recognised at national or at farm-level. Improvement in calf survival rates is dependent upon re-prioritization of this problem relative to other animal health and welfare issues and creation of awareness of this prioritization. Once the problem is recognised action needs to be taken at national and at farm levels, specifically on problem farms. Data recording, research, breeding, veterinary, extension and farmer organisations all have a role to play in improving bovine neonatal survival and hence improving animal welfare in the future. Ultimately improvements in welfare will be achieved by the aggregation of marginal gains across each of these inter-related disciplines.

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