

## Production diseases of the transition cow: Milk fever and subclinical hypocalcaemia

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### Introduction

Milk fever and subclinical hypocalcaemia (total blood calcium  $\leq 2.0$  mmol/l) are the most important macromineral disorders that affect transition dairy cows. It is important to realise, that of all the production diseases experienced by dairy cattle, milk fever is related to the occurrence of many other problems, the timing of which would suggest that milk fever was at least one (if not the only) predisposing factor that lead to a second transition or early-lactation cow disorder.

On average, 5-10% of dairy cows succumb to clinical milk fever, with the literature suggesting that the incidence rate in individual herds reaches as high as 34% (Houe et al., 2001). In Ireland, the Dairy Herd Health Group at UCD have recently encountered several cases where the incidence rate of clinical milk fever in individual dairy herds was 50% or more. Interestingly, Roche (2003) has reported an incidence rate of subclinical hypocalcaemia for grazing New Zealand dairy cows of 33%, where clinical milk fever incidence was only 5%. Unfortunately, there is no definitive data on the prevalence of subclinical hypocalcaemia in Irish dairy herds. However, if it is as prevalent here as it is in other countries, then control strategies must not focus solely on the five or so clinical cases in every 100-cow dairy herd.

### Why prevention strategies are essential

Farmers, veterinarians, nutritionists and other farm advisors often focus on outcomes, such as milk yield and fertility, in the absence of reviewing 'up-stream' factors such as management practices, nutritional regimes and health status of the herd. The occurrence of milk fever or subclinical hypocalcaemia is related to increased incidence rates of several other transition cow disorders. For example, it has been reported that milk fever cows are up to eight times more likely to develop mastitis in the following lactation, are three times more likely to develop dystocia and two to four times more likely to develop displaced abomasum. Therefore, it is of utmost importance that both milk fever and subclinical hypocalcaemia are prevented.

It is still quite common to find farms that have absolutely no control strategy in place for milk fever prevention. Many of these farms may escape for a good deal of time and then one important factor, such as an increase in grass availability or silage quality, will increase BCS (body condition score) at calving and result in a milk fever problem. It is the authors' view that good milk fever preventative strategies are essential on all farms. This paper discusses the consequences of milk fever and subclinical hypocalcaemia (Figure 1) and outlines some dietary control strategies that may be used to prevent them (Table I).

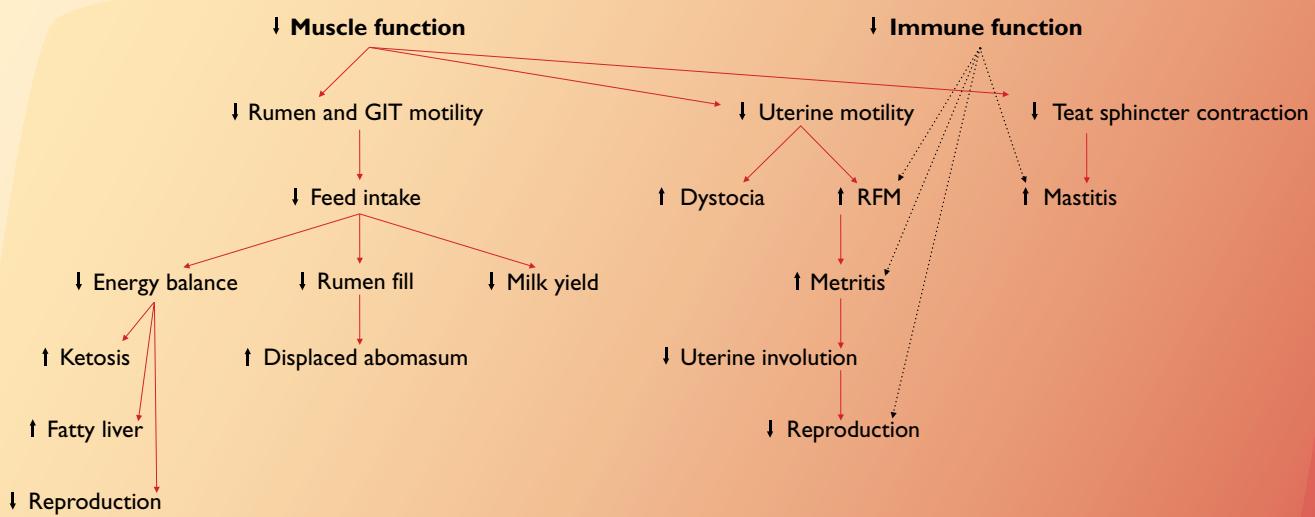


Figure 1: Consequences of milk fever and subclinical hypocalcaemia.

**Table I: Suggested criteria for the evaluation of milk fever prevention strategies**

BCS at 250 DIM	2.75
BCS at drying off	2.75
BCS at calving	3.0
Intake of Ca (g/d)	≤30
Diet P%	≤0.3% of DM
Diet Mg%	0.3 to 0.4% of DM
Diet K%	<1.8% of DM
DCAB	-100 to -200meq/kg DM
Blood Ca concentration 12-24hrs post-calving	>2.0mmol/l
Blood Mg concentration 24-48 hrs pre-calving	0.8 to 1.3mmol/l
Blood P (Inorganic P) concentration 12-24 hrs post-calving	1.4 to 2.5 mmol/l
Incidence of retained placenta in multiparous cows	<10%
Incidence of LDA in multiparous cows	≤3%
Incidence of dystocia in multiparous cows	<10%
Incidence of clinical milk fever	≤5%
Urine pH (if DCAB strategy used)	6.2 to 6.8 (Holstein cows)

Taken from Mulligan et al. 2006.

### Important physiological consequences of hypocalcaemia

It has been recognised for some time that milk fever and subclinical hypocalcaemia reduce the ability of the transition cow to effect smooth and skeletal muscle contraction. More recently it has been reported that both milk fever and subclinical hypocalcaemia exacerbate the level of immuno-suppression experienced by periparturient dairy cattle (Kimura et al., 2006). While it is difficult to explain precisely the aetiology of how milk fever results in the occurrence of several other transition cow disorders, these proven physiological phenomena of hypocalcaemic cows should always be borne in mind.

### Clinical consequences of hypocalcaemia

#### Dystocia and uterine prolapse

One can easily appreciate the problems that a reduced ability of smooth and skeletal muscle contraction might cause for cows in labour. Several published studies indicate an increased likelihood of dystocia in milk fever cows in comparison to normal cows. In some cases the increased odds of dystocia were reported as six times that of normal cows with other reports indicating an increased likelihood of around 2.5 to 3 times that of normal cows (Curtis et al., 1983; Erb et al., 1985; Correa et al., 1993). Apart from dystocia, it has been reported that cows suffering from uterine prolapse have a lower serum calcium (Ca) concentration than normal cows (Risco et al., 1984). Furthermore, in the latter publication, 19% of the cows suffering from uterine prolapse were classed as having severe hypocalcaemia (serum Ca <4mg/dl) while a further 28% of the affected cows were classed as having moderate hypocalcaemia (serum Ca 4.1 to 6.0mg/dl).

#### Retained placenta

Several studies have been cited that indicate increased risk for the occurrence of retained placenta following milk fever, with milk fever cows being up to three times more likely to experience retained placenta than normal cows (Houe et al., 2001). The direct effect of milk fever on the occurrence of retained placenta (excluding any interaction for the effect of milk fever on dystocia) has been reported to double the odds of retained placenta occurring (Erb et al., 1985). Furthermore there is also a large indirect effect of milk fever on retained placenta, as milk fever is a risk factor for dystocia, and dystocia is a risk factor for retained placenta (Correa et al., 1993). Recently, Melendez et al. (2004) have reported a significantly lower plasma Ca concentration in cows with retained foetal membranes in comparison to cows with normal placental expulsion. The point should also be made that, in this case, the hypocalcaemia experienced by cows with retained foetal membranes was subclinical not clinical. There is, therefore, a clear link between milk fever and the occurrence of retained placenta.

#### Endometritis

The clear links between milk fever, dystocia and retained placenta that have been discussed above, together with the reported link between milk fever and periparturient immuno-suppression, provide a strong basis for the suggested association between milk fever and endometritis (Kimura et al., 2006). In support of this, Whiteford and Sheldon (2005) recently observed a significantly higher incidence rate of endometritis in UK cows that suffered clinical hypocalcaemia in comparison to normocalcaemic cows.

Therefore, there are several reports in the literature linking milk fever with complications occurring at or around parturition. This fact

simply confirms what most people working with dairy cattle have probably already appreciated. However, it is very likely that many farm animal veterinarians deal with ongoing problems of retained placenta and poor fertility without considering milk fever and subclinical hypocalcaemia as possible predisposing factors. The reports above also underline the need for good milk fever control measures, especially as these complications at parturition are all likely to result in a lower reproductive efficiency and higher culling rates in dairy herds. Furthermore, it is very likely that subclinical hypocalcaemia will insidiously increase the predisposition of dairy cows to these conditions, again the need for a successful milk fever prevention programme to avoid this is paramount.

#### Milk fever and fertility

It has been suggested that milk fever results in reduced fertility in dairy cows due to its effect on uterine muscle function, slower uterine involution (Borsberry and Dobson, 1989) and reduced blood flow to the ovaries (Jonsson and Daniel, 1997). There are also indirect effects of milk fever on fertility, which are mediated through dystocia, retained placenta and endometritis. Whiteford and Sheldon (2005) reported that cows with clinical hypocalcaemia had a greater diameter of the gravid uterine horn and non-gravid uterine horn between 15 and 45 days post-partum (indicative of slower uterine involution) and a significantly reduced likelihood of having a corpus luteum (indicative of ovulation since parturition) than normal cows. Furthermore, Kamarpour *et al.* (1999) reported that subclinically hypocalcaemic cows have fewer ovulatory sized follicles at days 15, 30 and 45 post-partum and smaller follicles at first ovulation than normal cows. Other workers (Borsberry and Dobson, 1989) reported an increased number of services per conception (1.7 versus 1.2), an increased calving to first service interval (68 versus 61 days) and an increased calving to conception interval (88 versus 76 days) for milk fever cows, in five UK dairy herds with an incidence rate of clinical milk fever of 7.5%. Therefore, it is the authors' view that trying to improve fertility in Irish dairy herds without first having a good idea of transition cow health status, management and nutrition will bring limited improvements only.

#### Milk fever and mastitis

Curtis *et al.* (1983) reported that cows that had suffered clinical milk fever were eight times more likely to develop mastitis than normal cows. It has been hypothesised that the reasons for this phenomenon are (a) a reduction in smooth muscle function at the teat sphincter and hence an easy route for infection after milking and (b) an exacerbated suppression of immunity in milk fever cows when compared with normal cows (Goff, 2003). Cortisol is believed to be an important component of the suppressed immunity experienced by periparturient dairy cattle. It has been demonstrated that both milk fever and subclinical hypocalcaemia cause an increase in the normal cortisol response at parturition (Horst and Jorgensen, 1982). Furthermore, it has been recently demonstrated that hypocalcaemia is associated with reduced intracellular Ca stores in peripheral blood mononuclear cells and that this exacerbates periparturient immunosuppression (Kimura *et al.*, 2006). Therefore, the epidemiological association found between milk fever and the occurrence of mastitis is easily supported by several potential biological mechanisms, some of which have been reported as being more relevant in periparturient

dairy cows.

#### Milk fever and gastrointestinal tract function

Several authors have reported a reduction in the motility of the rumen and abomasum (Daniel, 1983, Jorgensen *et al.*, 1998) in subclinically and clinically hypocalcaemic cows. This reduction in ruminal and abomasal motility will likely cause a reduction in feed intake. This is particularly important in high producing dairy cows, as they are required to eat such large volumes of feed to meet their metabolic needs that physical limitation of feed intake is almost always significant. Therefore, the effect of milk fever or subclinical hypocalcaemia on rumen motility, which may last for the first week of lactation (Goff, 1996), may well exacerbate negative energy balance in cows that are already underfed. When this latter phenomenon is considered, it is of no surprise that an increased likelihood for the occurrence of ketosis following milk fever has been reported (Houe *et al.*, 2001). Furthermore, Goff (2003) has indicated that low plasma Ca concentration around calving will result in reduced motility and strength of abomasal contractions and hence abomasal atony and distension of the abomasum.

Therefore, milk fever has been implicated as a predisposing factor for many other transition cow disorders. It is difficult to think of any other factor that is associated with so many economically important veterinary complications of dairy cattle, particularly one that seems to sit as high as milk fever does in the cascade of possible events that cause problems for transition dairy cows.



Figure 2: Over-conditioned dry cows are four times more susceptible to milk fever than thinner cows.

## The prevention of milk fever and subclinical hypocalcaemia

### Body condition score (BCS) management

Achieving the correct BCS at calving and drying-off is critical for the prevention of milk fever. It has been reported that dairy cows that are over-conditioned at calving are up to four times more likely to develop milk fever (Ostergaard et al., 2003) (Figure 2). It is unclear why this is the case, but several hypotheses have been suggested to explain this effect. Firstly, it has been suggested that dairy cows with higher BCS at calving have a higher Ca output in milk, making them more prone to milk fever. Secondly, it is widely appreciated that over-conditioned dairy cattle have a reduced feed intake relative to thinner cows, in the last week or ten days pre-calving. This may reduce their intake of Ca and Mg to levels which predispose them to the development of hypocalcaemia. Finally, it has been shown, in human patients suffering from non-alcoholic fatty liver disease, that serum concentrations of 25-OH-vitamin-D3 are lower than healthy controls. Thus one wonders if over-conditioned dairy cows are capable of producing sufficient amounts of the active form of vitamin-D3 to prevent hypocalcaemia.

### Magnesium supplementation

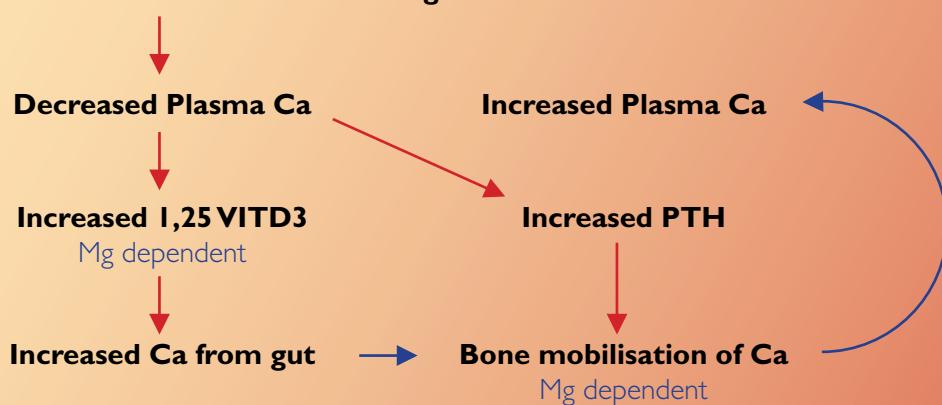
Ensuring adequate magnesium supplementation is vital for the prevention of milk fever. Magnesium (Mg) plays a very important role in Ca metabolism (Figure 3), for example it is a key intermediate in the resorption of Ca from bone by parathyroid hormone. In a recent review, increasing Mg supplementation was found to have the greatest influence amongst dietary strategies for the prevention of milk fever (Lean et al., 2006). Therefore, dietary Mg concentration for pregnant

dairy cattle should be in the region of 0.4% of dry matter (DM) (Goff, 2004; Lean et al., 2006). In order to feed Mg at 0.4% of DM for diets based on Irish grass and grass silage, approximately 20g of Mg needs to be supplemented pre-calving. This is based on the average Mg concentration of Irish grass of 0.2% and the average Mg concentration of Irish grass silage of 0.18% (Rogers and Murphy, 2000). Some of the mineral premixes currently sold in Ireland for pre-calving cows supply only 10–12g of Mg when fed at the recommended feeding rate. This will result in a Mg intake of around 0.3% of diet DM, which is not ideal, as Lean et al. (2006) reported that increasing Mg supplementation from 0.3 to 0.4% of the diet DM reduced milk fever incidence by 62%. To identify herds where the Mg feeding strategy is not optimal, blood Mg concentration may be determined in cows that are expected to calve in the next 24–48 hours (Whitaker, 1997). The ideal range has been reported as 0.8 to 1.3 mmol/l (Whitaker, 1997).

### Dietary cation anion balance (DCAB) and potassium

The concept of dietary cation (sodium and potassium) anion (chlorine and sulphur) balance  $\{(Na + K) - (Cl + S)\}$  has focused attention on the level of potassium (K) that is contained in the feed of pre-calving dairy cattle. It is now widely accepted that the homeostatic mechanisms that result in milk fever prevention work more efficiently when DCAB is negative. The most common strategy employed to achieve this negative DCAB is the addition of anionic salts to the diet of pre-calving cattle (Goff, 2004). Goff (2004) has stated that it is very difficult to control hypocalcaemia if total ration K is  $>1.8\%$ . Given that the average K values reported for Irish grass and grass silage are 2.9 and 2.3% (Rogers and Murphy, 2000), respectively, it will be difficult to achieve negative DCAB for many dairy farms. Some people in Ireland

### Excessive Ca loss in colostrum at calving



**Figure 3: Simple representation of calcium metabolism in the periparturient cow.**

do use DCAB strategies to prevent milk fever in dairy cows. It is important if using this strategy to use grass silage or grass where no K fertiliser or slurry has been recently applied. On the other hand, some Irish silages can be as low as 1% K, so it is probably best to have the forage tested for K if using this strategy. One of our foremost mineral premix manufacturers currently recommend testing urine pH in dry cows before implementing the DCAB strategy for milk fever prevention. For those using the addition of anionic salts to try and prevent milk fever and hypocalcaemia, it is important that (a) the DCAB for dry cows is between -100 and -200 meq/kg DM (Goff and Horst, 1997), (b) that urine pH for cows fed using the DCAB strategy is 6.0 to 6.8 and (c) that dietary Ca concentration is 1.2% of the diet (Ca sulphate and not Ca carbonate should be used) (Oetzel et al., 1988). The monitoring of urine pH for eight or more close-up cows fed using this DCAB strategy is extremely useful to determine if optimal dietary acidification has been achieved (Oetzel, 2004). It is also important to state that even if you are not using a strict DCAB strategy for milk fever prevention, reducing dietary K is advantageous for milk fever prevention in all circumstances (Lean et al., 2006). This is likely related to the reported reduction in milk fever incidence by reducing DCAB even if DCAB does not actually get negative (Lean et al., 2006) and also because K prevents Mg absorption from the gastrointestinal tract.

#### **Ca restriction and milk fever prevention**

One of the classical strategies often proposed for milk fever prevention is the restriction of Ca intake pre-calving. This has the effect of making sure that parathyroid hormone and the active form of vitamin-D3 are in higher concentrations in circulation on the day of parturition when Ca export in colostrum increases suddenly. This strategy does work, and recent data where Ca binders were used to block Ca uptake from the gut have shown a reduced milk fever incidence on several farms in New Zealand (Wilson, 2001). However, in practical situations it is necessary to achieve a Ca intake of 30g per day or less for this strategy to work. Irish grass and grass silage contain on average 6.5 and 6.9g of Ca per kg of DM. For a 600kg dry

cow consuming 1.8% of live weight as dry matter, this equates to a Ca intake of 70 to 75g per day. Therefore, Ca restriction is not a practical alternative for milk fever prevention on Irish farms using grass or grass silage as a large component of the dry-cow diet.

#### **Conclusions**

Milk fever and subclinical hypocalcaemia are the most important macromineral disorders of the transition cow. For several production diseases, complications of parturition and reproduction and also infectious diseases, milk fever seems to be implicated as being a predisposing factor at least in some cases. Milk fever and subclinical hypocalcaemia can to a large extent, be prevented by good dry cow management and appropriate nutrition.

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#### **Practical notes for the prevention of milk fever**

Shortfalls in the target incidence of milk fever, retained placenta, displaced abomasums, dystocia, downer cows, poor feed intake or poor reproductive efficiency in early lactation necessitate the consideration of milk fever and subclinical hypocalcaemia as contributing factors.

- BCS management is critical for the prevention of milk fever with the target BCS at calving of 3.0 being suggested. The BCS of all cows should be assessed at calving and at drying-off.
- The specific strategy for milk fever control on the farm should be identified. All farms should have some pre-determined strategy for milk fever prevention.
- A dietary Mg concentration of close to 0.4% should be achieved after consideration of the Mg in home grown forages and added Mg. In many cases, in Ireland, this will mean adding 20g of Mg to the diet from supplements.

- The authors of this review have found it useful to assess blood Mg concentration in cows that are within seven days of calving.
- It is vital that all cows have access to the minerals fed and that only palatable anionic salts are fed if they are to be used. Adequate feed availability is important in the immediate pre-calving period (last five days) if, for example, a substantial amount of the magnesium allowance for dairy cattle is supplied by the forages or mix fed.
- Many herd problems of milk fever in autumn calving cows are related to the grazing of cows on relatively high quality pasture in the close-up dry period. This pasture often contains a high concentration of N (nitrogen) and K, both of which reduce Mg uptake from the gut.
- It is important to restrict K intake for dry cows as part of a milk fever prevention programme.
- Target urine pH for cows fed using the DCAB strategy is 6 to 6.8. It is essential to monitor the urine pH of eight close-up dry cows if using the DCAB strategy.

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