

Metabolic diseases in dairy cows

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A combination of factors can often come together to induce a metabolic disease problem. The clinical cow we see is commonly just “the tip of the iceberg”, with many of her cohort being subclinical for the same condition.



Calcium and magnesium are both high turnover minerals, therefore intake is important.

Metabolic conditions include diseases such as:

- hypocalcaemia
- hypomagnesaemia
- hypophosphataemia
- ketosis
- fatty liver
- ruminal acidosis

It is not possible to discuss all of these in depth and [ketosis has been covered well in an article by Sara Pedersen](#), so I will look at the first three items and suggest the latter three headings could be considered as management diseases rather than metabolic diseases.

It is also worth noting many other conditions are linked with metabolic diseases/disturbances, including displaced abomasum, retained fetal membranes and metritis, and, although the links exist, a lot of work is still to be done to determine the details behind those links.

There are also many and varied methods for preventing metabolic diseases, but we need to understand the background to enable us to choose a suitable management plan for each farm as the right prevention is the one that will be used properly.

Hypocalcaemia

The mobilisation, absorption and utilisation of calcium (Ca) is controlled by parathyroid hormone (PTH), calcitonin and vitamin D metabolism.

Vitamin D stimulates Ca and phosphorous (P) absorption from the gut and resorption from bone, and promotes renal conservation of Ca. It is active when bound to receptor sites in the ruminal epithelium, intestine, bone and mammary, pancreatic and parathyroid glands. Vitamin D principally facilitates the absorption of Ca-binding protein, which transports Ca across the gut. While milk fever has been associated with vitamin D deficiency, milk fever incidence is most frequently associated with failure of Ca homeostatic mechanisms, even when vitamin D is adequate.

Most vitamin D is stored in the fat depots and the liver. An increase in PTH-induced hydroxylation of 25-hydroxycholecalciferol (25-HCC) in the kidney occurs in response to an increasing requirement for Ca and phosphate (PO₄) metabolism. Binding of PTH to membrane receptors on kidney cells stimulates 1 α -hydroxylase, which generates 1,25-dihydroxycholecalciferol (1,25-DHCC) up to a threshold level. Conversely, calcitonin suppresses the synthesis of 1,25-DHCC when blood Ca levels are more than adequate.

1,25-DHCC initiates transfer of Ca across the duodenal brush border by active transport. It is critical to the pathogenesis of milk fever that this transport mechanism requires stimulation by 1,25-DHCC for 16 to 24 hours to be activated. Similarly, bone resorption of Ca requires stimulation by both 1,25-DHCC and PTH for 48 hours.

Therefore, in early lactation, bone resorption of Ca lags behind intestinal transport mechanisms and both sources of Ca input lag behind the massive increase in Ca demand immediately postpartum. Logically, in cases of milk fever these responses are even more sluggish.

Bone resorption of Ca usually plays a minor role in Ca homeostasis until one to two weeks postpartum. However, when cows receive low Ca diets during the close-up dry period and/or when acidotic conditions are generated (as is the rationale behind negative dietary cation-anion balance; DCAB diets) bone Ca contributes significantly to the plasma Ca pool.

Milk fever is generally not related to inadequate production of PTH and 1,25-DHCC. Rather, 1,25-DHCC fails to stimulate the organs of the gut and bone rapidly enough to increase the rate of Ca input. Furthermore, intestinal 1,25-DHCC receptors in the cow decrease with age.

In addition, in older cows, fewer osteoclasts operate in response to PTH stimulation or an acidic

environment. Their bone responses are delayed and inadequate to rectify hypocalcaemia. However, about 10% of milk fever cows do have delayed or insufficient production of 1,25-DHCC and suffer relapsing milk fever. Cows that survive eventually produce sufficient 1,25-DHCC and recover.

The clinical signs of milk fever are the result of the effect of hypocalcaemia on the membrane potentials of excitable cells. Hypocalcaemia blocks transmission of nerve impulses through the neuromuscular junction because inadequate Ca availability blocks acetylcholine release. Low blood calcium also hinders Ca-dependent actin-myosin interactions and thereby decreases muscle contractility. With complete blockage of impulse transmission, flaccid paralysis occurs. Furthermore, a decrease in serum P and an increase in serum magnesium (Mg) concentrations, which occur in uncomplicated, textbook cases of parturient paresis, enhance this effect.

Panel 1. Blood testing reference ranges

Ca – 2.0mmol/L -3.0mmol/L*

Mg – 0.7mmol/L -1.3mmol/L*

P – 1.2mmol/L -2.3mmol/L*

Be aware Ca is not very useful except in very late pregnancy or early lactation.

P levels affected by haemolysis so preferred sample via oxalate-fluoride (grey top).

**reference ranges from Biobest Laboratories*

The important aetiological factors include:

- low calcium intakes (post-calving)
- it is a high turnover mineral that needs replacing – anything affecting rumen activity will also have a detrimental effect (acidosis)
- DCAB
- balance of sodium/potassium with chloride and sulphur (basic equation) targeting a zero or negative figure to help with acidification of the blood
- lack of Mg results in decreased release/action of PTH
- predisposing factors
- age, breed, parity and so on

Hypomagnesaemia

Hypomagnesaemia, otherwise known as grass tetany, affects lactating dairy and beef cows and, sometimes ewes, grazing grass pastures in southern Australia and New Zealand in autumn and winter.



Calcium levels drop precipitously around calving.

Hypomagnesaemia is the result of an imbalance between Mg inputs, dictated by dietary Mg intake, bioavailability and absorption, and outputs, mostly as a result of the large losses that occur through Mg secretion into milk.

Each kilogram of milk contains approximately 0.12mg Mg. Normal serum Mg concentration is between 0.7mmol/L and 1.3mmol/L. Mobilisation of body Mg reserves cannot maintain normal plasma Mg concentration in cattle in the face of high milk secretion and Mg deficient diets.

A decrease can result in a reduction in the concentration of Mg in the cerebrospinal fluid to below 0.5mmol/L, which leads to hyperexcitability, muscular spasms, convulsions and death from hypomagnesaemic tetany due to disturbances of neuromuscular transmission.

Low plasma Mg levels lead to failure of transport mechanisms for Mg to enter cerebrospinal fluid from blood. Ca homeostasis fails and hypocalcaemia occurs when blood Mg falls less markedly (to 0.6mmol/L to 0.75mmol/L). Blood calcium levels fall more rapidly when dietary intake of potassium is high. Low blood calcium triggers drainage of Mg from the brain, which precipitates grass tetany.

Thus, hypomagnesaemia and hypocalcaemia frequently occur concurrently, which tends to confuse the clinical signs presented. Severe hypomagnesaemia prevents production and secretion of PTH and 1,25-DHCC.

During hypocalcaemia, hormones elicited to correct the calcium imbalance increase blood Mg levels if dietary Mg is adequate. The kidney is the principal regulator of Mg homeostasis. PTH

raises the renal threshold for Mg reabsorption. However, it fails to raise blood concentrations of Mg if they fall below 0.7mmol/L.

1,25-DHCC also may play a role in ruminal Mg absorption, as the ruminal epithelium contains a 1,25-DHCC receptor site. In mature cattle, the stratified squamous epithelium of the reticulum, rumen and omasum is the major site of net Mg absorption. Mg is transported across the epithelium by an active sodium (Na)-linked, adenosine triphosphatase (ATP)-dependent pump, situated in the basal border of the cell. Small amounts of Mg are absorbed from the small intestine in the adult ruminant, while absorption in calves occurs primarily in the jejunum.

Cows older than six years are most commonly affected, particularly during lactation. Younger, two-year-old and three-year-old cows may be affected in herds with the more complex types of syndromes associated with high potassium (K) and low Na and P intakes.

The important aetiological factors include:

- **Low Mg intake** – a reduction in feed intake when cows are grazing short, grass dominant pastures, and where pastures contain less than 1.5g Mg/kg dry matter (DM).
- **High K and low Na intakes** – high K reduces the availability of Mg and dietary Na less than 2mg/kg DM reduces the absorption of Mg. This effect may be mediated via impairment of Na-dependent transfer of Mg across the ruminal mucosa. Be wary of the potential role of potash fertiliser in the aetiology of grass tetany.
- **The cow's ability to maintain Ca homeostasis** – cows with hypomagnesaemia do not develop grass tetany until blood calcium levels decrease.
- **P intake** – low rumen P concentrations have been shown to impair Mg absorption.
- **Rumen ammonia concentration relative to fermentable substrate** – high rumen nitrogen concentration and low water soluble carbohydrate intake predisposes ruminants to grass tetany. Synthesis of microbial protein decreases and excess nitrogen is diverted to ammonia production, which impairs Mg absorption.
- **Exposure to bad weather, which can reduce feed intake temporarily** – in cows and ewes of marginal Mg status this can be sufficient to precipitate grass tetany.

Hypophosphataemia

The common manifestations of P deficiency such as poor production, anoestrus and infertility relate to the many roles/essential substances that P is incorporated in within the body, such as nucleic acids and energy compounds like ATP and creatine phosphate. High maize silage diets may be low in P, as will be older senesced pastures.

The biochemical and physiological functions of P interrelate with vitamin D and Ca metabolism. Efficient P and Ca absorption requires adequate vitamin D. High dietary Ca intake depresses P absorption, whereas low P diets increase the efficiency of P absorption. This is mediated via

increased production of 1,25-DHCC in the kidney, which leads to more P being taken up by the mucosal cells of the small intestine.

1,25-DHCC stimulates P absorption independently of PTH, but PTH increases PO₄ diuresis. Ca intake, not P intake, controls PTH and 1,25-DHCC production. If cattle are grazed for prolonged periods on pastures that have adequate Ca and inadequate P, less 1,25-DHCC is produced by the kidneys and P absorption is decreased.

Animals deficient in P have marked demineralisation of bone. Hypophosphataemia is not known to have a stimulatory effect on bone resorption. Demineralisation during P deficiency is most probably due to a normal rate of osteoclastic activity without concurrent osteoblastic activity. Formation of organic bone matrix (osteoid) continues and replaces mineralised bone as it is resorbed. The result is soft bones prone to fracture (osteomalacia). In addition to excess osteoid, growing animals have failure of endochondral ossification.

There is debate around the involvement of P in the downer cow syndrome. Although cases of calcium deficiency that fail to respond initially to treatment may often respond when P is also given, this doesn't correlate with animals suffering prolonged P deficiency that fail to demonstrate recumbency (Radostits et al, 2000).

Macro-mineral interactions

- Uncomplicated cases of parturient paresis are best treated with Ca borogluconate, not with solutions that contain Mg since these cows are already hypermagnesaemic and excess Mg may compete with Ca for binding sites at the presynaptic membrane, thereby inhibiting acetylcholine release.
- Most uncomplicated cases of parturient paresis are hypophosphataemic, but P status is returned to normal when Ca status is corrected. Some cows that fail to respond will benefit from the administration of P.
- Frequently, pastures or forages that are low in Ca also predispose cattle to hypomagnesaemia and the presenting signs are often, therefore, a confusing combination of hypocalcaemia and hypomagnesaemia. In this situation, it is obviously logical to treat with solutions containing both Ca and Mg. Furthermore, Mg concentration does not drop precipitously until blood Ca concentration falls to a critical level, in which case a mixed solution is appropriate for a mixed pathology.
- Be mindful of the mineral status of cows treated for dystocia. If the cow is down and the calf is delivered readily by traction, the dystocia was most likely to be due to hypocalcaemia and the cow should be treated accordingly. In cases of difficult and/or prolonged deliveries or caesareans, particularly in inclement weather, assume the blood concentrations of the high turnover minerals Ca and Mg will be depressed and treat prophylactically.

To fully discuss some of the preventive options regarding the aforementioned metabolic diseases

would take considerably more space. If we refresh our memories of the background to the mechanisms taking place within the cow this provides us with a basis from which to advise on the treatment of clinical cases and also to think a little more closely about the control measures we may want to put in place.

References

- Radostitis OM et al (2000). Metabolic diseases. In *Veterinary Medicine: A Textbook of the Diseases of Cattle, Sheep, Pigs, Goats and Horses* (9th edn) Saunders: 1,417-1,475.

Further Reading

- Chamberlain AT and Wilkinson JM (2005). *Feeding the Dairy Cow*, Chalcombe Publications.
- Chamberlin WG et al (2013). Subclinical hypocalcaemia, plasma biochemical parameters, lipid metabolism, postpartum disease, and fertility in postparturient dairy cows, *Journal of Dairy Science* **96**(11): 7,001-7,013.
- DeGaris PJ and Lean IJ (2008). Milk fever in dairy cows: a review of pathophysiology and control principles, *Veterinary Journal* **176**(1): 58-69.
- Kronqvist C et al (2011). Effects of prepartum dietary calcium levels on calcium and magnesium metabolism in periparturient dairy cows, *Journal of Dairy Science* **94**(3): 1,365-1,373.
- Oetzel GR (1991). Meta analysis of nutritional factors influencing milk fever in dairy cattle, *Journal of Dairy Science* **74**(11): 3,900-3,912.