

# Calcium and Magnesium Disorders



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## KEYWORDS

• Milk fever • DCAD • Hypomagnesemia • Hypocalcemia • Parathyroid hormone

## KEY POINTS

- Hypocalcemia is a clinical disorder that can be life threatening to the cow (milk fever) and predisposes the animal to various other metabolic and infectious disorders.
- Calcium homeostasis is mediated primarily by parathyroid hormone, which stimulates bone calcium resorption and renal calcium reabsorption.
- Parathyroid hormone stimulates the production of 1,25-dihydroxyvitamin D to enhance diet calcium absorption.
- High dietary cation-anion difference interferes with tissue sensitivity to parathyroid hormone.
- Hypomagnesemia reduces tissue response to parathyroid hormone.

## IMPACT OF HYPOCALCEMIA ON COW HEALTH

Total blood calcium (Ca) concentration in the adult cow is maintained between 8.5 and 10.0 mg/dL (2.1 and 2.5 mmol/L). Nearly all cows will experience some degree of hypocalcemia at the onset of lactation; however, the severity and duration of the hypocalcemia experienced depends on the integrity of the cow's Ca homeostasis mechanisms. Typically, the nadir in blood Ca concentration occurs 12 to 24 hours after calving. Surveys in the United States suggest around 5% of cows will develop milk fever each year<sup>1</sup>; the incidence of subclinical hypocalcemia (blood Ca values between 5.5 and 8.0 mg/dL [1.38–2.0 mmol/L] during the periparturient period) is around 50% in older cows.<sup>2</sup> Cows with subclinical hypocalcemia mobilize more body fat resulting in higher blood nonesterified fatty acid concentrations, increasing the risk for ketosis and displaced abomasum. Hypocalcemia reduces rumen and abomasal motility, further increasing the risk of abomasal displacement. Hypocalcemia also

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Author Disclosures: Before joining the faculty at Iowa State University, J.P. Goff was Director of Research at West Central Farmer's Cooperative. In this capacity, he developed anion supplements for prevention of hypocalcemia in cows and continues to consult for this company. J.P. Goff also holds a patent using calcium propionate paste to prevent hypocalcemia. Department of Biomedical Sciences, College of Veterinary Medicine, Iowa State University, 2048 Vet Med, Ames, IA 50011, USA  
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reduces the contraction of the teat sphincter muscle responsible for closure of the teat orifice after milking, thus, increasing the risk of mastitis. Hypocalcemia is accompanied by reductions in intracellular endoplasmic reticulum and mitochondria stores of Ca in blood mononuclear cells. Low intracellular stores of Ca impair the immune cell response by reducing the release of the second messenger Ca into the cytosol from intracellular stores in response to cytokines, antigens or other activating stimulus.<sup>3</sup> Martinez and colleagues<sup>4</sup> found that subclinical hypocalcemia impaired many aspects of neutrophil function, and cows with subclinical hypocalcemia had higher blood  $\beta$ -hydroxybutyrate concentrations than normocalcemic cows. They also concluded the relative risk of developing metritis increased by 22% for every 1 mg/dL decrease in serum Ca less than 8.59 mg/dL. Subclinical hypocalcemia increases the risk for fatty liver development and reduces fertility of the cow.<sup>5</sup> Milk fever and subclinical milk fever should be considered gateway diseases that greatly reduce the chance for full productivity of a cow in the ensuing lactation.

## CA HOMEOSTASIS

### *Ca Pools Within the Body*

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Blood Ca in the adult cow is maintained between 8.5 and 10.0 mg/dL (2.1–2.5 mmol/L). About 50% of the Ca is bound to proteins such as albumin, and 42% to 48% of the Ca exists in the ionized form. The ionized Ca concentration is the biologically active portion of the Ca in blood. Under acidic conditions, the ionized portion of Ca in the blood is closer to 48%; under alkaline conditions, it is closer to 42% ionized. The final 3% to 7% of Ca in blood is bound to soluble anions, such as citrate, phosphate, bicarbonate, and sulfate. If total serum proteins are greatly reduced (hypoalbuminemia), it is possible to have low total Ca in the blood and relatively normal levels of ionized Ca in the blood. Serum albumin does decline slightly at calving; but this is not a major concern in periparturient cows, and this author thinks there is little to be gained clinically by adjusting blood Ca concentration for albumin content. Recent advances in ion electrode design are making cow-side ionized Ca determinations practical, though total Ca concentration determinations are as useful clinically.

There are 3.0 to 3.5 g of Ca in the plasma pool and another 8 to 9 g of Ca in all the extracellular fluids (outside of bone) of a 600-kg cow (Fig. 1). Between 7.8 and 8.5 kg of Ca is contained within the skeleton. Less than 1 g of Ca is stored inside of all the cells of the body. Dairy cows producing colostrum (containing 1.7–2.3 g of Ca per kilogram) or milk (containing 1.1 g of Ca per kilogram) withdraw 20 to 30 g of Ca from these pools each day in the first days of lactation. In many cows, the demand for Ca increases dramatically even before calving, as Ca leaves blood and is sequestered within the mammary gland during colostrum formation. If the cow is to avoid severe or prolonged hypocalcemia at the onset of lactation, she must replace the extracellular Ca that is used to produce milk.

### *Role of Parathyroid Hormone*

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Ca homeostasis is primarily controlled by the parathyroid glands, which are exquisitely sensitive to a decline in blood Ca concentration and respond to hypocalcemia by secreting parathyroid hormone (PTH). The parathyroid cells can determine the extracellular ionized Ca concentration using Ca sensing receptor molecules, located on the surface of parathyroid cells, which have the ability to bind ionized Ca in the millimolar range. Whenever ionized Ca in the extracellular fluid decreases below the concentration needed to keep the Ca sensing receptors fully occupied, PTH is secreted in large amounts.<sup>6</sup> PTH is an 84 amino acid peptide that binds to receptors located on the

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