VARIABILITY IN THE CONCENTRATION OF MINERALS IN BLOOD OF PERIPARTUM COWS

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Introduction

Transition cows rapidly undergo changes in intakes and outputs of mineral elements. Compared to the amount of nutrients transferred to the late-term fetus (House and Bell, 1993), the relative amounts of Ca, P, and Mg needed for synthesis of 15 kg of colostrum are 3.3-, 2.5-, and 7.5-fold higher. When faced with changing intake and demand for mineral elements, cows attempt to maintain relative uniformity in blood concentrations of mineral elements by a combination of variable intestinal absorption, urinary loss, endogenous loss, tissue deposition, and secretion into milk (Figure 1; Table 1). However, parturition disrupts many of the control mechanisms because in addition to the abrupt increases in nutrient needs, parturition also changes hormonal levels and gene expression.

Macrominerals

Often we think of minerals as either being under tight homeostatic control, in which there is little change in their blood concentration, or under loose homeostatic control, in which there are much wider swings in blood concentrations. For example, blood Ca concentration normally deviates little from 9.5 mg/dL because parathyroid hormone (**PTH**) and calcitonin respond to small changes in blood Ca, whereas blood inorganic P (**Pi**) varies diurnally between 4.0 and 6.5 mg/dL (Forar et al., 1982). The magnitude of the variation in plasma Pi is partially a function of dietary P intake. Although PTH increases urinary loss of P, normal changes in blood Pi have little effect on PTH.

Plasma Ca concentrations are reduced in early post-partum cows (Figure 2) because of increased demand of Ca for synthesis of milk coupled with the relatively slow response in up-regulating Ca absorption from the intestinal tract. The post-partum depression in plasma and ionized Ca is greater in older cows than in primiparous cows (Szenci et al., 1994). Although total plasma Ca is commonly measured in cows, an alternative measurement is ionized Ca in plasma. Ionized Ca is blood Ca that is not protein bound and is more readily transferred to tissues. The advantage to measuring ionized Ca is that it tends to be less variable than total plasma Ca (Szenci et al., 1994).

Table 1. Criteria for classification of adult cattle on Ca, Pi, and Mg concentrations in serum (Puls, 1988).

Status	Ca, mg/dL	Pi, mg/dL	Mg, mg/dL
Deficient	1 to 6	<0.5 to 4.5	<1.1
Marginal	7 to 9	4.0 to 4.6	1.2 to 1.8
Adequate	8 to 11	4.5 to 6.0	1.8 to 3.5
High	>12	8.0 to 12	> 4.0

An important function of Ca is enabling muscle contraction (Wilde, 2006). The post-partum drop in blood Ca in cows reduces the number and amplitude of ruminal

contractions (Figure 3; Daniel, 1983), which reduces feed intakes (Figure 4). One method to help minimize peripartum changes in Ca and Pi in blood is to adjust the cation-anion difference in dry cow diets (Table 2).

Table 2. Effect of prepartum dietary cation anion difference on plasma Ca and Pi in cows at 7 d post-partum (Gant et al., 1999).

	-10 to 1 d prepartum		7 d post-partum	
	Prepartum DCAD, mEq/100g DM			
	+53.1	*-8.5*	*+53.1*	*-8.62*
Ca, mg/dL	8.67	8.43	8.23	8.62
Pi, mg/dL	5.79	6.16	4.33	5.40

In addition to lower plasma Ca in fresh cows, plasma Pi also tends to be lower (Figure 2; Table 2). There are several contributing factors to post-partum reduction in plasma Pi. First, milk contains 0.09% P, hence there is increased need for P. A cow producing 100 lb of milk/day secretes 41 g of P daily in milk. Secondly, higher PTH levels, induced by low plasma Ca, increase urinary loss of P. Finally, lower feed intakes in peripartum cows reduce the amount of P absorbed from the intestinal tract.

The elevated serum Mg in cows with hypocalcemia (Figure 2) may be due to a combination of greater Mg mobilization from bone, reduced Mg uptake by cells, and reduced urinary Mg loss. In contrast, a deficiency of Mg reduces PTH secretion and 1,25 dihydroxy vitamin D_3 synthesis by the kidneys. Serum Mg also is depressed by large intakes of K and N, and also by high ruminal fluid pH. Sulfur concentrations in plasma also are depressed at calving (McAdam and O'Dell, 1982).

Trace elements

Nutritional status, based upon plasma concentration of trace elements, is given in Table 3. Intestinal absorption plays an important role in homeostatic control regulation of Zn and Cu. For example, entry of zinc (Zn) into the intestinal mucosa stimulates synthesis of metallothionein, which can bind Zn until the mucosal cell is sloughed. Likewise, the concentration of Zn in mucosal cells regulates Zn transporters that help deliver Zn to the serosal side of the mucosa for uptake on available binding sites on albumen. Thus, there are 3 regulatory points for Zn transfer into blood, and further mechanisms to reduce blood Zn concentrations via stimulation of interleukins and **ZIP**s (a family of Zn transporter proteins) for greater Zn transport into cells.

Changes in trace element concentrations in blood of peripartum cows are not uniform across herds. The late-term fetus accumulates Zn at a rate of about 12 mg/d (House and Bell, 1993), whereas 15 kg of colostrum contains about 285 mg Zn (Kincaid and Cronrath, 1992). This rapid need for Zn in synthesis of colostrum may explain why Zn concentration is 22% lower in blood of cows on day of calving. In addition, glucocorticoids reduce Zn absorption and combine with various stressors to stimulate metallothionein synthesis, which pulls Zn into cells. Infections (mastitis or metritis) will cause an initial drop in plasma Zn, which is subsequently followed by increased plasma

Zn. Neither change in plasma Zn reflects nutritional Zn status. In addition, the effect of Zn deficiency to reduce feed intake in cattle is seen before there is a drop in plasma Zn, hence, concentrations of plasma Zn in peripartum cows need to be partially interpreted in context of the cow's health.

Table 3. Criteria for classification of cattle on trace element concentrations in blood (Kincaid, 2000).

Status	Zn µg/mL plasma	Cu µg/mL plasma	Se µg/mL serum	Mn ng/mL serum	I µg/100 mL	B_{12} ng/L serum
Deficient	0.2 to 0.4	<0.2 to 0.5	<0.025	< 5	1-5	100
Marginal	0.5 to 0.8	0.5 to 0.7	0.03 to 0.06	5 to 6	5-10	100-200
Adequate	0.8 to 1.4	0.7 to 0.9	0.08 to 0.3	6 to 70	10-40	>200
High	2 to 5	0.9 to 1.1	> 2.5		70-300	
Toxic	3 to 15	>1.2	>3.5			

Newborn calves have very high concentrations of liver Cu compared to adult cattle (Kincaid, 2000). Placental transfer of Cu from the cow to the fetus accounts for much of the decline in plasma Cu concentration during late gestation (Xin et al., 1993). Another level of blood Cu regulation is variable endogenous loss. In addition to the regulation of Cu absorption from the intestinal tract, chaperone proteins in the liver deliver Cu to sites for endogenous excretion via bile. Unfortunately, in sheep this mechanism does not appear to operate well.

Cobalt and vitamin B_{12} concentrations also change in blood of peripartum cows (Kincaid and Socha, 2007). Serum vitamin B_{12} concentrations are reduced at dryoff (Figure 4), most likely the result of lowered feed intakes during the dry period compared to lactation, reducing subsequent ruminal B_{12} synthesis and intestinal absorption. Post-partum reductions in serum B_{12} reflect a deficit in ruminal B_{12} synthesis relative to B_{12} secretion into milk. As mid-lactation progresses, feed intakes increase, milk yields decrease, and serum B_{12} concentrations increase.

Concentrations of Se in blood often decline during late parturition with the magnitude of the decline being inversely related to Se intake, i.e., there is greater decline in blood Se of cows consuming less than 4 mg Se/d than cows consuming about 6 mg/Se d during late gestation (Table 4).

Table 4. Effect of Se supplementation during the dry period on the concentration of Se in cows < 8 h post-partum (Abdelrahman and Kincaid, 1995).

	Start 60 d prepartum			**End** < 8 h post-partum		
	Control 0.3 ppm Se	*+ 0.3 mg Se/d*	*SE*	*Control 0.3 ppm Se*	*+ 0.3 mg Se/d*	*SE*
Blood Se, µg/mL	0.146	0.151	0.005	0.106	0.134	0.003

Pregnant cows effectively transfer Se to their fetus (Table 5), thus, helping to prevent white muscle disease in newborn calves but putting themselves at greater risk for retained placenta and mastitis. Dry cows need Se intakes of > 4 mg/d to transfer sufficient Se (40 μg/d) to the fetus for liver Se in newborn calves to exceed 2.2 μg/g, DM, a level considered necessary for newborn calves (Kincaid, 1995). After parturition, serum Se increases slightly (~15%) in cows by 1 week after parturition (Gant et al., 1998) presumably because Se intakes increase. Increased feed intake means more Se is available for absorption from the intestinal tract.

Table 5. Blood glutathione peroxidase and liver Se in cows and calves

	Liver Se	GPX1
	μg/g, DM	*EU/mL*
Dam	>1	> 140
Newborn	2.2 to 7	250

Oxidative stress

Another factor affecting blood Se in post-partum cows is the increased reactive oxygen species (**ROS**) that are generated during weight loss. Antioxidant vitamins help reduce ROS, however, vitamin A, vitamin E, and β carotene are markedly reduced in blood of peripartum cows with β carotene concentrations reaching a nadir at about day 4 post-partum (Figure 5; Johnston and Chew, 1984; Goff and Stabel, 1990). The ROS act on promoter regions of genes to increase synthesis of many selenoproteins as well as metallothionein. Hence, metabolism of both Se and Zn is affected by ROS generated during weight loss in early lactation. Sordillo et al. (2007) recently reported changes in activity of selenoproteins in peripheral blood mononuclear cells of peripartum cows (Table 6). Whereas activity of GPX1 increased in post-partum cows, activity of thioredoxin reductase (a selenoprotein) was reduced. The loss of body weight in early postpartum cows, increases generation of ROS and hydroperoxides, and chemical reduction of ROS may deplete GSH (reduced glutathione) in PBMC, thus accounting for the changes in peripartum activities of GPX1 and thioredoxin reductase. Similarly, we (unpublished results) have recently found that mRNA levels for selenoprotein W, but not GPX1, increase in skeletal muscle of cows during weight loss.

Table 6. Oxidative stress in periparturient cows (Sordillo et al., 2007)

	Lactation stage		
Parameter	C –20 d	C –0 d	C +21 d
GPX1, mU/μg protein	95[a]	157[a,b]	200[b]
Plasma lipid hydroperoxides, nmol	200[b]	300[a]	280[a]
GSH, μM	533[a]	488[a]	342[b]
GSH:GSSH ratio	547[a]	171[b]	575[a]

[a,b] Means followed by different superscripts differ, $P < 0.05$.

Sample type and collection method

Whether whole blood, plasma or serum is sampled can affect interpretation of results. The slow turnover of red blood cells makes whole blood unresponsive to short-term changes in Se intake. Therefore, plasma Se is often measured because it better reflects recent intakes of Se. Blood monocytes also may be a useful measure of Se status (Sordillo et al., 2007). Serum Cu values are ~14% lower than plasma Cu values (Kincaid et al., 1986). If cattle are consuming Mo, then plasma (and serum) needs to be treated with TCA prior to analysis to precipitate that Cu complexed with Mo. The type of anti-coagulant affects the concentration of Zn, and rubber stoppers contaminate with Zn as well. Because red blood cells have higher concentrations of P, Fe, Zn, Se, and Mn than plasma, hemolysis will inflate plasma values for these elements.

Summary

The concentration of minerals varies in blood of peripartum cows as a result of changes in dry matter intake, the concentration of nutrients in the diet and interactions between those nutrients, transfer of nutrients to the fetus, initiation of milk synthesis, changes in hormone levels and body weight loss. A key component of mineral metabolism in peripartum cows is preventing hypocalcemia, which reduces dry matter intake (DMI) and increases risk of health disorders. Transition diets may need higher amounts of minerals (and vitamins) to prevent low blood concentrations of nutrients in cows. Reduced blood concentrations of many nutrients (Se, Cu, Zn, Vit A, and Vit E) are correlated with lowered measures of immunity, increased incidence of mastitis, and other health problems. In the future, nutrigenomics and metabolomics may combine data on blood concentrations of minerals with information on the variation of the genome of the cow and her physiological state to allow development of supplementation programs that maximize milk production while minimizing risk of health disorders and nutrient excretion.

Figure 1. Dynamics of minerals in blood. Additional factors that affect minerals in blood are fasting, infection, oxidative stress, glucocorticoids, hormones, and interactions with other nutrients.

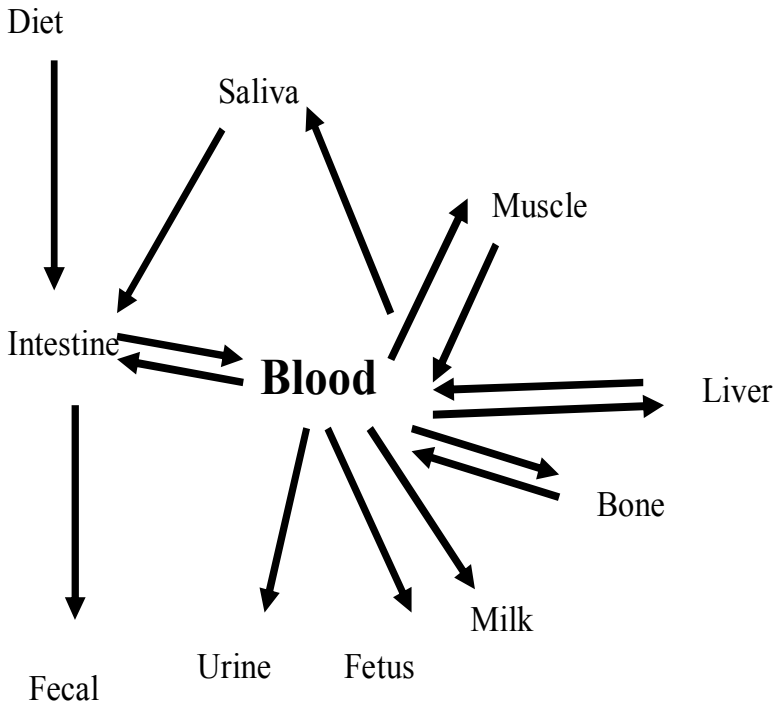


Figure 2. Effect of hypocalcemia on Ca, Pi, and Mg in plasma of peripartum cows (Marquardt et al., 1977).

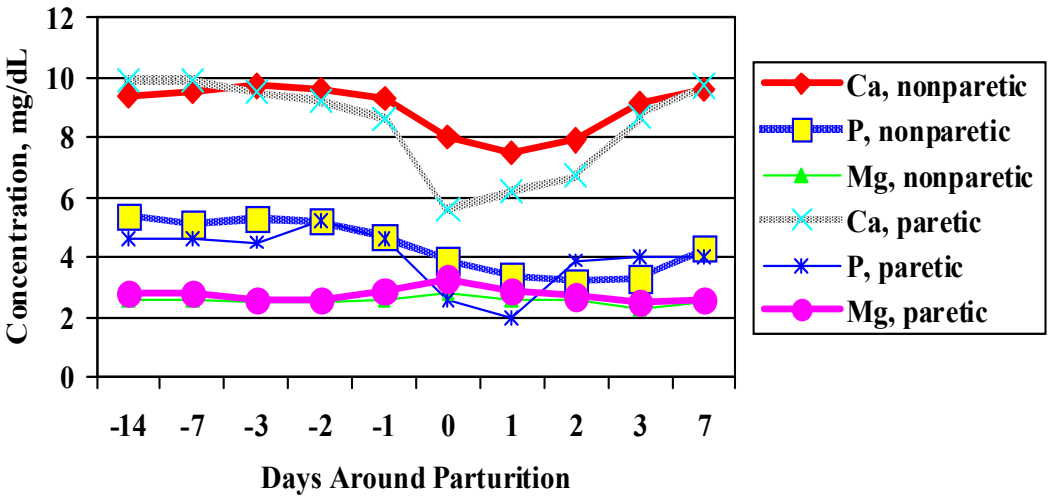
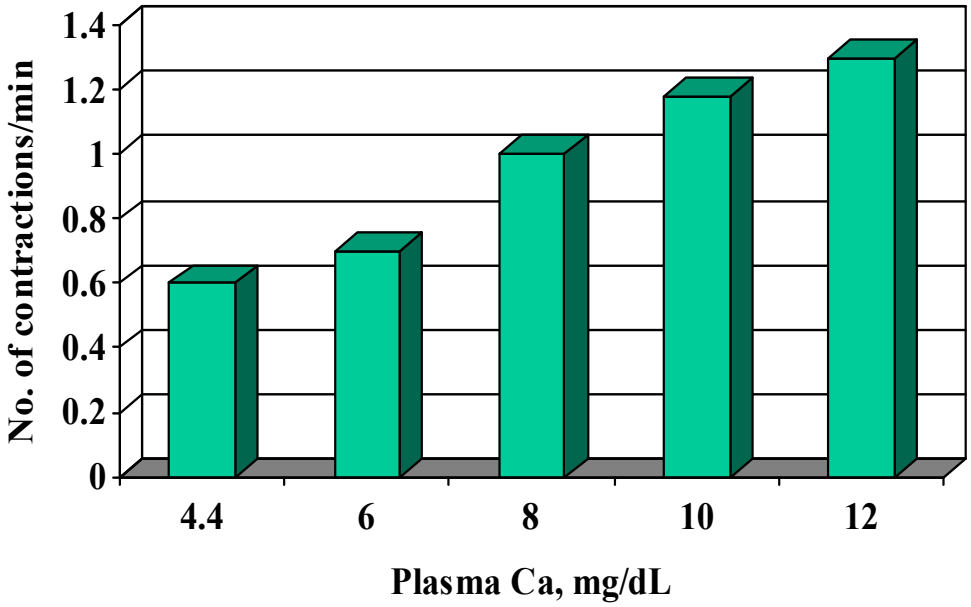


Figure 3. Relationship between plasma Ca and ruminal contractions (Daniel, 1983)



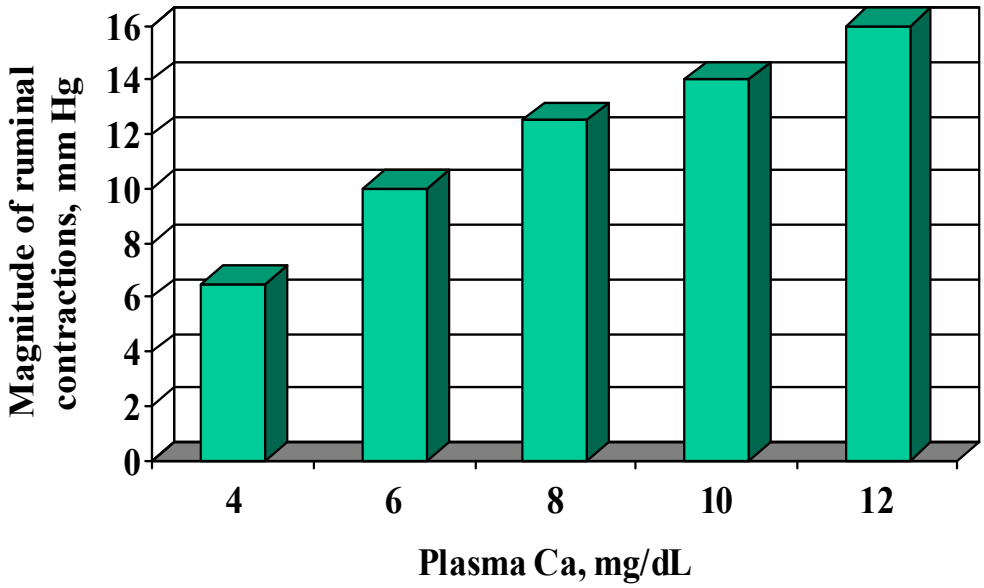


Figure 4. Effect of hypocalcemia on dry matter intake of peripartum cows (Marquardt et al., 1977).

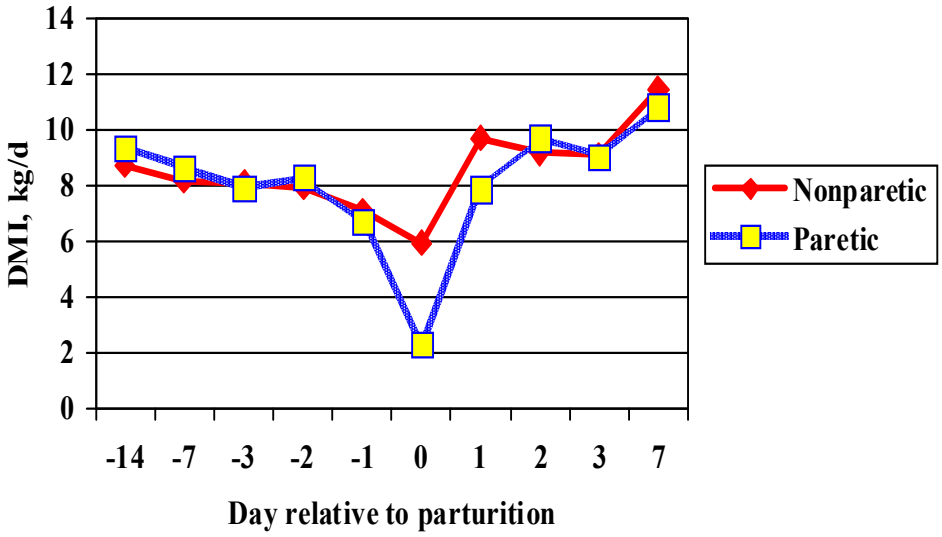
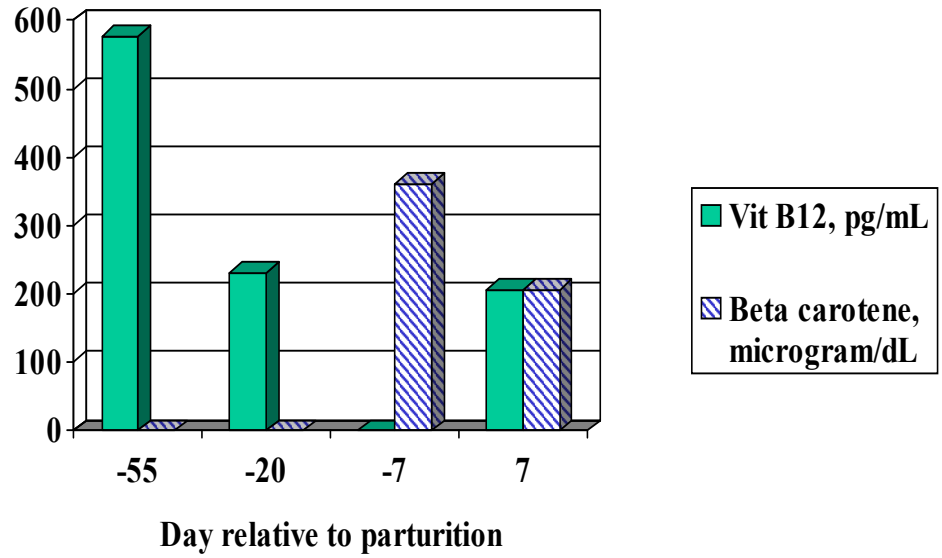


Figure 5. Peripartum changes in vitamin B_{12} and β carotene in blood of peripartum cows (Kincaid and Socha, 2007; Johnston and Chew, 1984).



References

Abdelrahman, M. M., and R. L. Kincaid. 1995. Effect of selenium supplementation of cows on maternal transfer of selenium to fetal and newborn calves. J. Dairy Sci. 78:625-630.

Daniel, R. C. W. 1983. Motility of the rumen and abomasum during hypocalcaemia. Can. J. Comp. Med. 47:276-280.

Forar, F. L., R. L. Kincaid, R. L. Preston, and J. K. Hillers. 1982. Variation of inorganic phosphorus in blood plasma and milk of lactating cows. J. Dairy Sci. 65:760-763.

Gant, R. G., W. Sanchez, and R. L. Kincaid. 1998. Effect of anionic salts on selenium metabolism in nonlactating pregnant dairy cows. J. Dairy Sci. 81:1637-1642.

Goff, J. P., and J. R. Stabel. 1990. Decreased plasma retinol, α-tocopherol, and zinc concentration during the periparturient period: effect of milk fever. J. Dairy Sci. 73:3195-3199.

House, W. A., and A. W. Bell. 1993. Mineral accretion in the fetus and adnexa during late gestation in Holstein cows. J. Dairy Sci. 76:2999-3010.

Johnston, L. A., and B. P. Chew. 1984. Peripartum changes of plasma and milk vitamin A and β-carotene among dairy cows with or without mastitis. J. Dairy Sci. 67:1832-1840.

Kincaid, R. L. 2000. Assessment of trace mineral status of ruminants: a review. Proc. Am. Soc. Anim. Sci. 1999. Avail at: http://www.org/jas/symposia/proceedings/0930.pdf.

Kincaid, R. L. 1995. The biological basis for selenium requirements of animals. The Prof. Anim. Sci. 11:26-29.

Kincaid, R. L., and J. D. Cronrath. 1992. Zinc concentration and distribution in mammary secretions of peripartum cows. J. Dairy Sci. 75:481-484.

Kincaid, R. L., C. C. Gay, and R. I. Krieger, 1986. Relationship of serum and plasma copper and ceruloplasmin concentrations of cattle and the effects of whole blood sample storage. Am. J. Vet. Res. 47:1157-1159.

Kincaid, R. L., and M. T. Socha. 2007. Effect of cobalt supplementation during late gestation and early lactation and serum measures. J. Dairy Sci. 90:1880-1886.

Marquardt, J. P., R. L. Horst, and N. A. Jorgensen. 1977. Effect of parity on dry matter intake at parturition in dairy cattle. J. Dairy Sci. 60:929-934.

McAdam, P. A., and G. D. O'Dell. 1982. Mineral profile of blood plasma of lactating dairy cows. J. Dairy Sci. 65:1219-1226.

Puls, R. 1988. Mineral Levels in Animal Health. Sherpa International, Clearbrook, B.C. Canada

Sordillo, L. M., N. O'Boyle, J. C. Gandy, C. M. Corl, and E. Hamilton. 2007. Shifts in thioredoxin reductase activity and oxidant status in mononuclear cells obtained from transition dairy cattle. J. Dairy Sci. 90:1186-1192.

Szenci, O., B. P. Chew, A. C. Bajcsy, P. Szabo, and E. Brydl. 1994. Total and ionized calcium in parturient dairy cows and their calves. J. Dairy Sci. 77:1100-1105.

Wilde, D. 2006. Influence of macro and micro minerals in the peri-parturient period on fertility in dairy cattle. Anim. Repro. Sci. 96:240-249.

Xin, Z., D. F. Waterman, R. W. Hemken, and R. J. Harmon. 1993. Copper status and requirement during the dry period and early lactation in multiparous Holstein cows. J. Dairy Sci. 76:2711-2716.