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ORIGINAL CONTRIBUTION

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Animal nutrition and acid-base balance

Summary In domestic animals, acid-base balance may be influenced by nutrition. The major research effort in this area has been made on the prevention of hypocalcemic postparturient paresis in dairy cows. This disorder is caused by the sudden increase of calcium secretion into the colostrum. The manipulation of the dietary cation-anion difference makes it possible to maintain the cows in metabolic acidosis during the critical period that precedes calving, presumably via a mechanism that involves the strong ion difference in the extracellular fluid. As a consequence the mobilization of calcium is enhanced and the incidence of the disorder is decreased. Conversely, a dietary induced metabolic alkalosis leads to a more severe degree of hypocalcemia and the incidence of the disease is increased. The underlying mechanisms of the prevention are only partially understood. Nevertheless, this preventive method is already widely applied in practice. Nutrition effects on acid-base balance also influence growth and food intake in higher vertebrates and fish. As a consequence, the incidence of developmental orthopedic diseases in fast-growing domestic animal species may be affected. Also, the bone mineral content of athletic horses may be influenced by dietary induced modification of the acid-base status. The mineral loss due to metabolic acidosis may lead to an increase in the incidence of stress fractures. This overview should give insight into relevant aspects of nutrition and acid-base balance in domestic animal species.

Key words DCAD – Animal – Cow – Acid-base balance – Hypocalcemia – Growth

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Introduction

Nutrition may profoundly influence acid-base balance in domestic animals. An important practical application is the manipulation of the diet in order to prevent the hypocalcemic postparturient paresis of dairy cows. This disease is responsible for major economic losses and a sound strategy for its prevention is of foremost importance. For that reason a substantial research effort was made and is still continuing in order to understand the pathophysiology of this disorder and the mechanisms by which dietary prevention functions. Furthermore, growth of several species was found to be affected by dietary induced metabolic acidosis or alkalosis. Another area which has been only partly explored is the high incidence of stress fractures in athletic horses which may be explained in part by the ingestion of acidogenic diets. This overview should give insight into relevant aspects of nutrition and acid-base balance in domestic animal species.

Prevention of hypocalcemic postparturient paresis of dairy cows

Calcium homeostasis in the periparturient period of dairy cows

The calcium (Ca) homeostasis of mainly high-yielding high-parity dairy cows is very often disturbed by a sudden increase in demand for Ca at the initiation of lacta-

tion [1–4]. During the dry period, only the Ca lost due to the fetal and endogenous fecal drain (2 to 7 and 5 to 7 g/Ca per day, respectively) has to be replaced and the mechanisms for replenishing plasma Ca are thus relatively inactive (Fig. 1). Because the cow's milk contains 1.2 g Ca/L [5, 6], more than 25 g of Ca is needed in the Ca pool during lactation (Fig. 2). At parturition, the Ca demand of cows, especially of high yielding animals, suddenly increases because of secretion of Ca into the colostrum which contains approximately 2.3 g Ca/L. Thus, a cow producing 10 L of colostrum loses about 23 g of Ca in the first single milking. This amount of Ca is about nine times higher than that present in the entire plasma Ca pool (2.5–3 g) and more than two times that present in the extracellular pool (9 to 11 g). The Ca that is absorbed from the ingested food is momentarily insufficient to replace this loss. As a result, hypocalcemia develops and the cows begin measures to increase serum Ca concentration by enhancing its reabsorption from the renal tubules, its mobilization from the bone reserves and its absorption from the intestinal tract (Fig. 3) [1–4, 7–9]. Clinical symptoms of this disease include inappetence, inhibition of urination and defecation, paresis, lateral recumbency and eventually coma and death. If left untreated, the outcome is death in approximately 60 to 70 % of the cases. This disorder affects three to eight percent of the cows worldwide and is a major cause of loss of productivity and increased predisposition to secondary diseases. Also, subclinical hypocalcemia influences the incidence of many periparturient disease such as dystocia, retained placenta, displacement of the abomasum, uterine prolapse, metritis and mastitis. The economical impact of postparturient subclinical hypocalcemia is important in the dairy business, and major efforts were thus undertaken in order to find adequate methods for the prevention of the disease. Beside pharmacological doses of Ca and vitamin D or its metabolites, nutrition strategies have been developed. The dietary content of Ca, P and Mg are known to play a non-negligible role in the incidence of clinically manifested hypocalcemia [4]. A major development which has already found a broad application in practice is the control of acid-base balance by modification of the dietary cation-anion difference (DCAD) [10]. The underlying mechanism of this strategy is only partially understood.

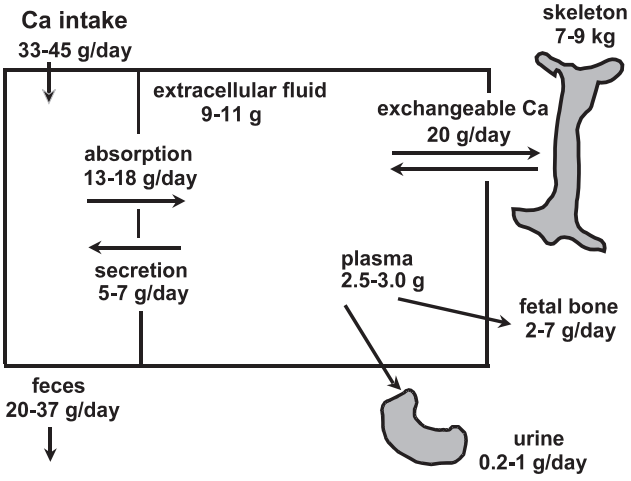

Fig. 1 Calcium homeostasis in a 500-kg cow during the dry period.

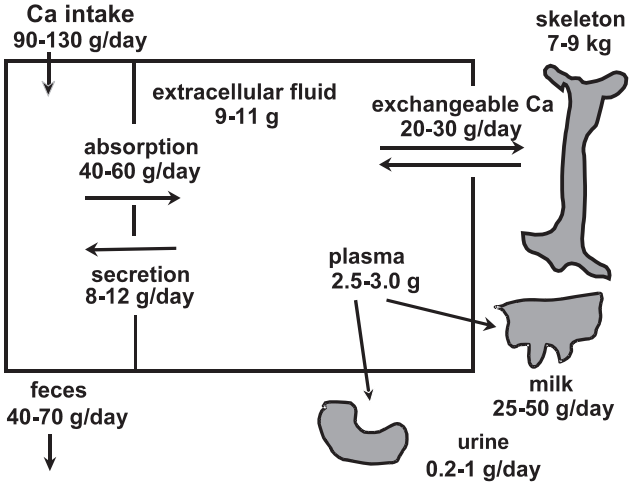

Fig. 2 Calcium homeostasis in a 500-kg cow during lactation.

Dietary cation-anion difference

Early in the 20th century, the composition of dietary ash was recognized to profoundly affect the acid-base balance of the human body [11]. In the 1960s, reports from

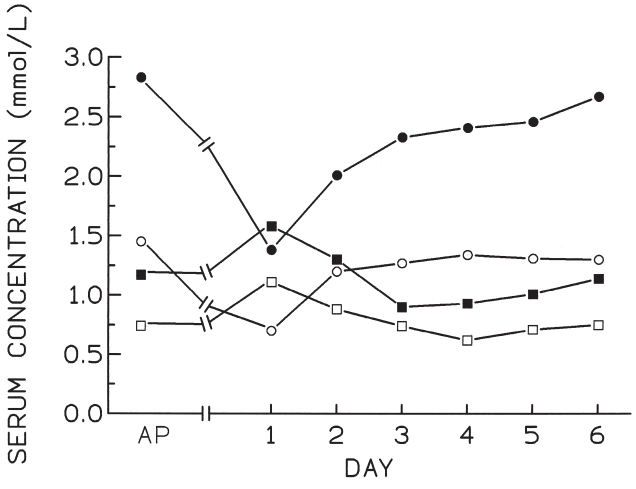

Fig. 3 Serum concentrations of Ca_{tot} (●), Ca^{2+} (○), Mg_{tot} (■), and Mg^{2+} (□) in one 8-year-old Brown Swiss cow during the periparturient period (Reproduced from [8]).

Norwegian researchers pointed to the importance of the alkalinizing or acidifying effects of feedstuffs and sulfuric and hydrochloric acid on the incidence of postparturient paresis in dairy cows [12–15]. It was later confirmed that the disease is more prone to develop in cows which ingest an alkalogenic diet during the last three to five weeks of pregnancy. Diets high in cations, especially sodium (Na^+) and potassium (K^+), tend to induce postparturient paresis, whereas diets high in anions, primarily chloride (Cl^-) and sulfate (SO_4^{2-}), prevent it. The pre-fresh alkalogenic diet should be consumed for a minimum of 5 days before the actual calving [10]. Because the calving date may not be predicted with accuracy, a 21-day pre-fresh period is necessary to ensure that nearly all of the cows spend at least five days on the pre-fresh diet. A meta-analysis including the data from 75 published trials with a total of 1165 cows, 214 of which developed milk fever, revealed that prepartum dietary concentrations of SO_4^{2-} and dietary DCAD [DCAD = $(Na^+ + K^+) - (Cl^- + SO_4^{2-})$] were the two nutritional factors most strongly correlated with the incidence of postparturient paresis (Fig. 4) [16]. The analysis was done using a backward multiple logistic regression procedure. However, the model fit poorly. Reanalysis of the data using another model still recognized the importance of SO_4^{2-} but failed to confirm a role for DCAD [17].

Several theories have been proposed to explain how alkalosis or acidosis may be induced by the diet [18–20]. A comprehensive approach to acid-base balance which is commonly known as quantitative analysis of acid-base status was proposed in the early 1980s [21]. Instead of focusing exclusively on the equilibrium of carbonic acid, as traditional methods do, quantitative analysis seeks to study all the variables that influence the acid-base status. This comprehensive approach requires distinction between independent and dependent variables involved in acid-base balance. The independent factors responsible for changes in acid-base status are the following: the partial pressure of carbon dioxide, the strong ion difference and the total weak acid (mainly proteins) concentration. The term strong ions refers to the highly dissociated nonmetabolizable ions. The difference between the total number of strong cations and anions in the blood is thus called the strong ion difference. All the other variables commonly used for acid-base estimation (e. g., pH or bicarbonate) are dependent variables which change only when one or more of the independent variables are modified. According to this theory, in any given solution, including body fluids, the number of moles of positively charged particles (cations) must equal the number of moles of negatively charged particles (anions) and the product of the concentration of hydrogen ions (H^+) and hydroxyl ions (OH^-) must always be equal to the dissociation constant of water (approximately 1×10^{-14}). Both equations must be satisfied simultaneously. Because pH is the negative log of the concentration of H^+, this implicates that the pH of a solution is dependent on the difference between the number of negatively and positively charged particles in the solution. If positively charged particles are added to a solution, such as the plasma, the number of H^+ cations decreases and the number of OH^- anions increases in order to maintain the electroneutrality of the solution (the solution becomes more alkaline). Conversely, adding anions to a solution causes an increase in H^+ and a decline in OH^- in order to maintain electroneutrality and the pH of the solution decreases. Strong ions enter the blood from the digestive tract, making the strong ion difference of the diet the ultimate determinant of the blood strong ion difference. Once absorbed, the concentration of strong ions in the blood is regulated by the kidneys. Adjustment of the strong ion difference of the blood is slower than the respiratory control of blood pH but is capable of inducing much greater changes in blood pH.

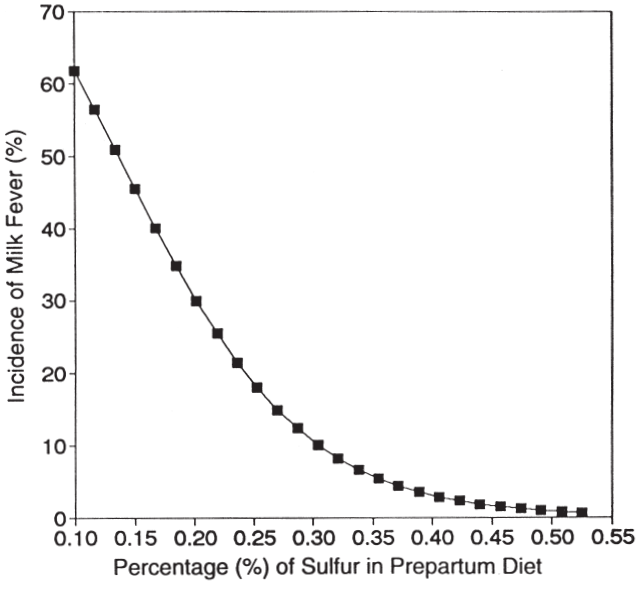

Fig. 4 Sample relationship of dietary SO_4^{2-} to the incidence of milk fever using the final regression model of a meta-analysis (Reproduced with permission from [22]).

Major advances have been made in the understanding of the influence of nutrition of acid-base balance on the basis of, among others, the metabolism of organic acids and the gastrointestinal absorption of alkali and acids [19, 20]. Organic acids knowingly consume bicarbonate in the reaction: organic acid + HCO_3^- → organic anion + CO_2. If the organic anion is retained in the body and is subsequently metabolized, there is no net loss of alkali. In this case, bicarbonate is regenerated as shown in the reaction: organic anion + H_2CO_3 → HCO_3^- + organic acid → HCO_3^- + CO_2 + H_2O. When the organic anion is not metabolized, either because it cannot be metabolized or because it is excreted in the urine, it represents a net loss of alkali. The ingestion of a nonab-

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sorbable or poorly absorbable cation accompanied by an absorbable anion and vice versa may strongly influence the acid-base balance. For example, the ingestion of $CaCl_2$ leads to a net loss of alkali, whereas the ingestion of $CaCO_3$, Ca acetate or Ca citrate leads to a gain of alkali. It is thus possible to explain in part the DCAD concept in dairy cows by the assumption that when the ingestion of nonmetabolizable cations is accompanied by metabolizable anions, the subsequent absorption and metabolism of their anions results in a gain of alkali, and that ingestion and absorption of nonmetabolizable anions accompanied by metabolizable cations would lead to a gain of acid. The difference between the two represents a net gain of alkali. In the diet of cows, K^+ salts are represented in the largest amount (up to 5%).

In theory, all the cations and anions in the cows' diet are capable of exerting an influence on the strong ion difference of the blood [4, 10, 22, 23]. The major cations present in feeds and the charge they carry are Na^+ (+1), K^+ (+1), Ca^{++} (+2), and Mg^{++} (+2). The major anions found in feeds and their charges are Cl^- (–1), SO_4^{2-} (–2), and $H_2PO_4^-$ (assumed to be –3). Cations or anions present in the diet will only alter the strong ion difference of the blood if they are absorbed into the blood. The trace elements present are absorbed in such small amounts that they are of negligible consequence to acid-base status. Organic acids, such as the volatile fatty acids, are generally absorbed in the undissociated form so that they carry both the positive and negative charge into the blood. They are also rapidly metabolized in the liver, so they have only a small effect on blood pH under most circumstances.

The difference between the number of cations and anions absorbed from the diet determines the pH of the blood. The concentrations of these ions are most commonly expressed as milliequivalents per kilogram. This value is usually calculated from just Na^+, K^+, Cl^-, and SO_4^{2-} concentrations as follows:

$$DCAD = (Na^+ + K^+) - (Cl^- + SO_4^{2-}) \quad (1)$$

This equation is useful, although it must be kept in mind that Ca, Mg, and P absorbed from the diet also influence blood pH. Correcting for the absorption rate, the following equation is obtained:

$$(Na^+ + K^+ + 0.38\ Ca^{++} + 0.30\ Mg^{++}) - (Cl^- + 0.60\ SO_4^{2-} + 0.60\ H_2PO_4^-) \quad (2)$$

It is assumed that Na^+, K^+ and Cl^- are absorbed with 100% efficiency. Correcting for the relative acidifying activity of various anionic salts by feeding them to dry cows and evaluating their ability to reduce urine pH:

$$(Na^+ + K^+ + 0.15\ Ca^{++} + 0.15\ Mg^{++}) - (Cl^- + 0.25\ SO_4^{2-} + 0.50\ H_2PO_4^-) \quad (3)$$

A complete equation should probably also include ammonium, because this cation seems to contribute to the cation content of the blood as well. Eq. (1) has become the standard for calculating DCAD.

Urinary pH is the indicator used in clinical practice to evaluate the effect of DCAD [24, 25]. The normal pH of bovine urine, like the urine of all herbivores, is greater than 8. The urinary pH of dairy cows on high strong-cation diets is generally above 8.2 and it may be reduced with anions to values around 5.5 (Fig. 5) [10]. For optimal control of subclinical hypocalcemia and milk fever, the average pH of the urine of Holstein cows should between 6.2 and 6.8. In Jersey cows which are more prone to develop hypocalcemia, these values should be 0.5 unit lower. If the average pH is between 5.0 and 5.5, the excessive amount of anions have induced an uncompensated metabolic acidosis and the cows will suffer a decline in dry matter intake.

Using Eq. (1), most typical diets fed to dry cows have a DCAD of about 100 to 250 mEq/kg of diet dry matter. Addition of anions to the diet to reduce DCAD is limited because of problems with palatability of the anionic salt

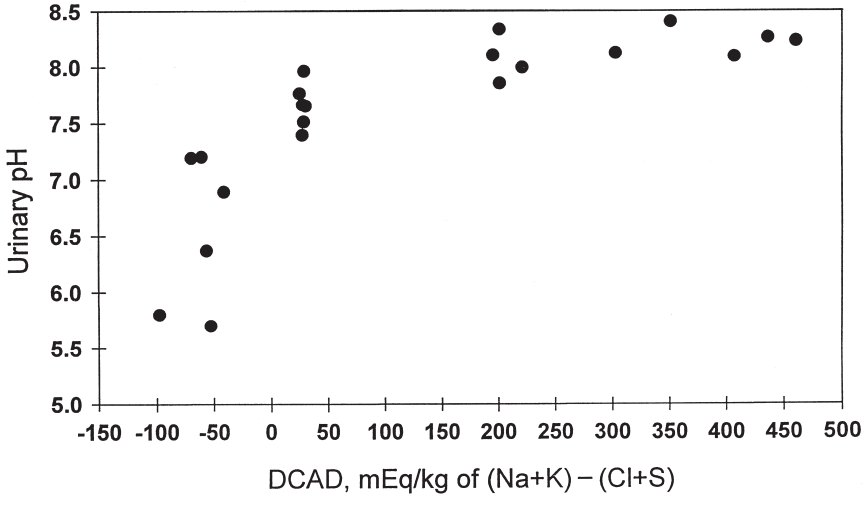

Fig. 5 Effect of dietary cation-anion difference (DCAD) of pre-fresh dairy cows (3 weeks prior to their due date). Each data point is the mean urinary pH of a group of cows fed a diet of known mineral content. *Na* sodium; *K* potassium; *Cl* chloride; *S* sulfur (Reproduced with permission from [10]).

sources commonly used. The actual strategy to prevent postpaturient paresis, thus, consists in reducing the K^+ content of the food and correcting if necessary the DCAD with Cl^- and SO_4^{2-} to an ideal value of –150 mEq/kg [3, 26]. This requires choosing the appropriate feedstuffs with low K^+ content, reducing heavy fertilization of the soil with K^+, manipulating the K^+ concentration in plants by selective breeding and harvesting alfalfa at more mature stages [3]. The tendency exists in industrial countries to perpetuate the accumulation of K^+ in the soil and the average K^+ concentration in legume forages may reach up to 5 %.

Effects of chronic metabolic acidosis on bone and on the calcium balance

Bone is involved as a buffering system for acid-base control of body fluids [27, 28]. Thus, acidifying diets induce the release of cations (including Ca) into the blood in order to correct its pH. Metabolic acidosis first stimulates the physicochemical mineral dissolution then the cell-mediated bone resorption by increasing the activity of osteoclasts and decreasing the activity of osteoblasts [29–32]. Parathyroid hormone (PTH) further augments the effects of metabolic acidosis on bone cells. Before calving, the plasma hydroxyproline concentration, a marker of bone resorptive activity, is higher in cows ingesting a diet rich in anions [26, 33]. In lambs fed diets containing 1 % ammonium chloride (NH_4Cl), increased tartrate-resistant acid phosphatase and decreased alkaline phosphatase activity in ribs indicated increased osteoclast and decreased osteoblast activity [34]. If the cows are in positive balance, the extra Ca entering the extracellular fluid Ca pool is excreted in urine (Fig. 6). Addition of anions to the diet of cows may increase the urinary Ca excretion from less than 0.1 g/day up to around 12 g/day [35]. Ca reabsorption in the renal tubule is directly inhibited in metabolic acidosis which leads to increased urinary Ca excretion [36, 37]. The increased bone resorption could thus be in part the consequence of the increased urinary Ca loss with subsequent decreased serum Ca concentration and increased PTH and $1,25(OH)_2D$ in order to maintain serum Ca concentration. In some studies, the Ca apparent absorption in the gastrointestinal tract is not influenced by the acid-base status [35], whereas in other studies Ca is more efficiently absorbed in the intestine of cows on acidogenic diets [38, 39]. However, no measurements on transepithelial Ca fluxes have been carried out in individual segments of the alimentary tract in animals receiving acidogenic or alkalogenic diets. Therefore, these observations suggest that the mechanism by which the anionic diets work in cows is by inducing a Ca release of up to around 12 g/day from bone into the extracellular fluid Ca pool or eventually by increasing the Ca apparent intestinal absorption. Ca exists within bones in two states: the overwhelming majority is tightly bound to the organic bone collagen matrix as $CaHPO_4$ deposits, and a small amount of Ca exists in solution in the fluids surrounding the bone cells and within the canaliculi of the bone [28]. The soluble Ca in the bone fluids is separated from the extracellular fluids of the body by a syncytium of bone-lining cells, some of which are osteoblasts and their precursors which seem to form a bone membrane. It was hypothesized earlier that upon stimulation by PTH, this bone fluid can be rapidly transferred into the extracellular pool by the bone-lining cells. However, the lining cells do not form a tight membrane covering bone surfaces (Fig. 7) [40]. These cells are separated by relatively open channels. This implies that bone fluid is a part of the extracellular fluid and not a separate compartment. PTH and calcitonin affect intracellular and extracellular aspects of the environment on bone surfaces. How these actions control plasma Ca concentra-

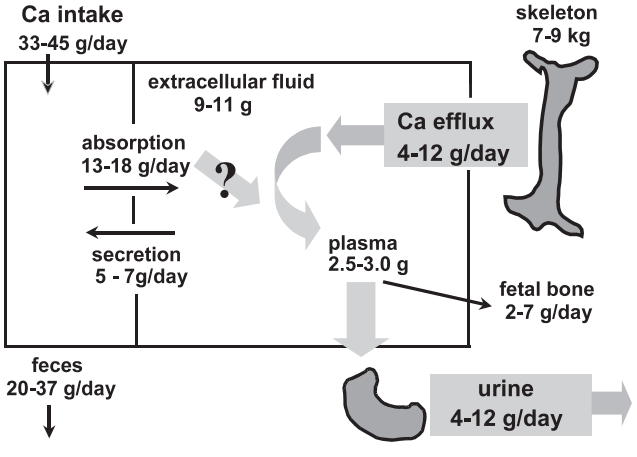

Fig. 6 Calcium homeostasis in a 500-kg cow during the dry period with a metabolic acidosis induced by a low cation-anion difference.

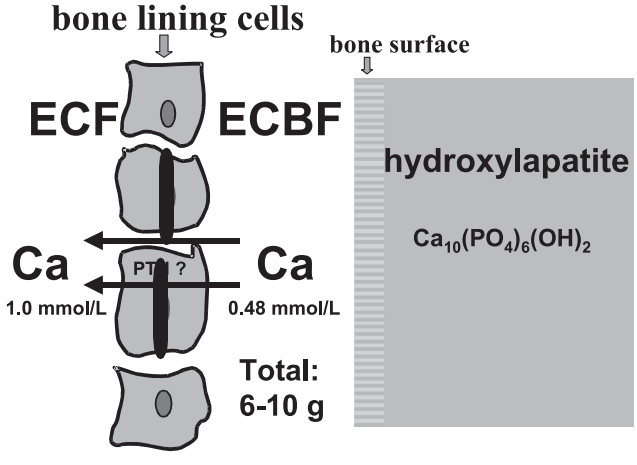

Fig. 7 Schematic representation of Ca repartition in bone.

tions has still to be fully explored. Based on the magnitude of the difference in serum Ca concentrations (which is in the range of 1×10^{-3} M) compared to the solubility of hydroxyapatite crystals (1×10^{-4}), the major mechanism controlling serum Ca seems to occur in the absence of PTH [40]. Bone surface proteins, particularly osteonectin and osteocalcin recognized as Ca binding proteins, and the hydration shell of hydroxyapatite may play a non-negligible role in the mobilization of Ca. The size of the readily exchangeable bone Ca pool in the adult cow has been estimated to be between 6 and 10 g of Ca, assuming that the total extracellular fluid Ca pool consists of about 8 to 10 g of Ca [41]. The amount of readily exchangeable bone fluid Ca can be increased 5 to 6 g by feeding ammonium chloride to induce metabolic acidosis. This observation is supported by the fact that more disodium ethylenediaminotetraacetate (Na_2-EDTA) may be infused in cows on anionic diets [42, 43]. The mechanism by which this occurs is unknown. It may be hypothesized that more Ca is available due to increased activity of osteoclasts or that metabolic acidose induces a conformational change of the bone surface protein resulting in a decreased amount of bound Ca. Finally, more Ca originating from the hydroxylpapatite crystals is released upon activation of osteoclasts (Fig. 8) [9]. This process is initiated on the second day after parturition, reaches a peak between 4 and 9 days after calving and is maintained during lactation [9, 44]. Also after at least two days, an increased amount of Ca is absorbed from the gastrointestinal tract in order to support the production of milk [45].

With hypocalcemia induced by intravenous administration of Na_2-EDTA, a dramatic reduction of Ca release into urine occurs in cows on an acidogenic diet [43], implying increased renal tubular reabsorption of Ca which is mediated by PTH. Thus, upon parturition, the ensuing lactational drain of Ca is most likely partially replaced by renal tubular resorption of Ca originating from bone. In laboratory animals, whether PTH has an anticalciuric effect during metabolic acidosis is controversial [36, 46]. Although a fraction of these 12 g of Ca may be resorbed from the urine, this amount appears to be a small amount relative to the total Ca lost into colostrum. However, it should be kept in mind that the standard treatment for milk fever consists of 8 to 12 g of Ca administered subcutaneously and intravenously, and that this small amount results in a clinical cure in most cases.

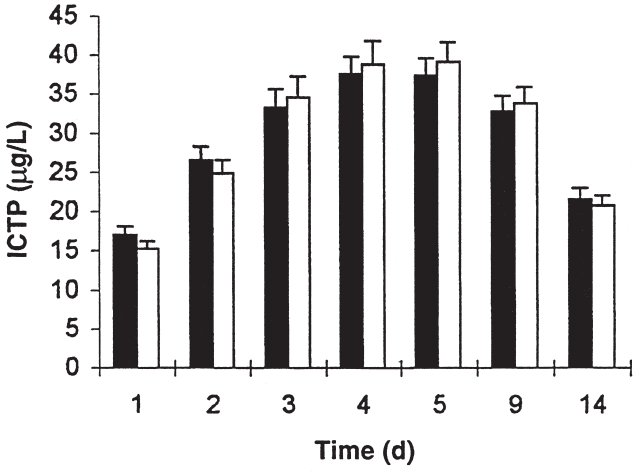

Fig. 8 Serum carboxyterminal telopeptide of type I collagen (ICTP) concentrations on the day of parturition on day 2, 3, 4, 5, 9, 14 after parturition for cows with (■; n = 18) and without (□; n = 19) periparturient paresis (Reproduced from [9]).

Effects of DCAD on PTH and 1,25(OH)$_2$D

In the cows ingesting anionic diets, the hypercalciuria induced by the metabolic acidosis directly maintains the concentrations of PTH and 1,25(OH)$_2$D at a level higher than before parturition [34, 37, 47, 48]. However, as reported for laboratory animals and humans, a direct effect of metabolic acidosis on the concentrations of PTH and 1,25(OH)$_2$D is difficult to assess due to the presence of confounding factors such as hypercalciuria, hyperphosphatemia and hypomagnesemia [27, 49].

Circulating concentrations of PTH and 1,25(OH)$_2$D were found to be higher in the blood of cows with postparturient paresis than in the blood of cows without postparturient paresis [50, 51]. It has been suggested that a mild metabolic acidosis increases tissue responsiveness to PTH [26, 33, 51]. This hypothesis was based on the observation that addition of anions to the diet increased osteoclastic bone resorption and synthesis of 1,25(OH)$_2$D$_3$ in cows [47, 48]. Indeed, cows fed a diet high in K^+ and Na^+ before parturition had lower plasma 1,25(OH)$_2$D concentrations at parturition despite more severe hypocalcemia. Both of these physiologic processes are controlled by PTH. Although still indirect, these data support the hypothesis that the receptors for PTH on the surface of bone and kidney cells are less able to function at high blood pH [3, 4]. Without a functional receptor, PTH can not work on the tissues, and Ca homeostasis is compromised. Further support of this hypothesis exists in direct studies of PTH responsiveness in rats and dogs [36, 52] which indicate that bone and perhaps renal tissues are refractory to the effects of exogenously administered PTH in the alkaline state and that the stimulatory effects of PTH are enhanced during metabolic acidosis. However, recent investigations demonstrated that acidosis also induced alterations in gene expression in osteoblasts [29, 53]. Osteoblastic immediate early response genes are inhibited as are genes controlling matrix formation. Thus, cellular mechanisms further down than the PTH receptor may explain the acidosis-induced modification in cell activity.

DCAD and performance of lactating cows

Not only the improvement of hypocalcemia obtained by adjustment of the DCAD is beneficial for optimizing milk yield during lactation. Dry matter intake and milk yield are positively influenced by alkalogenic diets [54–60]. Manipulation of the DCAD during lactation may prove useful in attenuating acid or base challenges on specific feeding regimens as, for example, a high-concentrate diet for a high-producing cow which will induce acidosis due to increased lactate production in the rumen.

Growth/developmental orthopedic disease

Chronic metabolic acidosis exerts an anti-anabolic effect in bone growth centers in vitro in mice which may explain the disturbance of longitudinal growth [61]. The cultured murine mandibular condyle system as a model for the skeletal growth center revealed that, after chronic exposure to an acidic medium, the expression of the insulin-like growth factor-I and growth hormone receptors was reduced resulting in an adverse effect on cellular differentiation. In support of these findings, decreased growth rate was observed in premature infants and newborns with prolonged maximum renal acid stimulation and late metabolic acidosis and other well-known clinical disorders produced by chronic acid loading [62–64]. However, the pathophysiology of growth failure is complex and the isolation of the effect of chronic metabolic acidosis itself is difficult.

Diets with a high DCAD inducing an alkalosis stimulate growth in lambs, calves, piglets, broilers and fish [65–70]. However, the effect on growth may be the consequence of higher feed intake, possibly by a direct effect on brain areas controlling feed intake. In swine, feed intake and growth are decreased with dietary induced metabolic acidosis [66].

The incidence of developmental orthopedic disease (DOD) in several animal species is related to rapid growth which is influenced by nutritional factors [71–74]. For example, one of the major factors associated with a high incidence of DOD in giant dogs is a high dietary intake of calcium [75–78]. It is presently unknown to which extent the alkalinizing or acidifying properties of food influence the incidence or severity of DOD in mammals. In poultry, dietary induced metabolic acidosis is associated with an increase in the incidence of tibial dyschondroplasia, and metabolic alkalosis with a decrease [74].

Non-structural carbohydrates and acid-base balance in ruminants and horses

Ruminants fed high-energy diets based on cereals such as corn or barley are characterized by a lower blood pH [79, 80]. High starch intake in ponies and horses reduce cecal and large colon pH relative to animals fed high roughage diets [72, 81–83]. The increase in H^+ ion concentration in the extracellular fluid is subsequent to increased fermentative activity in the rumen or in the large intestine of horses which induces an increased production and absorption of lactic acid, acetate and propionate.

Nutrition and acid-base status in athletic horses

The influence of DCAD and non-structural carbohydrate on acid-base balance, on mineral homeostasis and mineral excretion has received attention from equine researchers [72, 84, 85]. Rations with a DCAD less than 100 mEq/kg feed DM are acidogenic and result in enhanced calcium excretion. Diets fed to most horses have a calculated DCAD near 150 mEq/kg diet dry matter and may be as low as 100 mEq/kg dry matter (DM). Prolonged consumption of an acidogenic diet may lead to significant demineralization of bone and subsequent weakening of the skeleton. The effect of dietary induced metabolic acidosis has an inconsistent effect on the urinary excretion of phosphorus, potassium and magnesium. Ratios with a DCAD over 200 mEq/kg feed DM minimize the urinary calcium and phosphorus losses. Most grains contain a low DCAD (< 100 mEq/kg feed DM) and high concentrations of soluble, easily fermentable starch. High level performance horses and rapidly growing foals are commonly fed diets which contain > 50 % of the total ration by weight in the form of grain concentrate. A correct manipulation of acid-base balance may permit effective dietary prevention of stress fractures in race horses. The dietary cation-anion difference needs to be carefully considered when formulating rations to meet the Ca requirements. A correct adjustment of the acid-base balance by dietary means may also be beneficial to horse performance [72, 86, 87].

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