Bovine Acidosis: Implications on Laminitis

JAMES E. NOCEK
Agway Research Center Research and Development, Tully, NY 13159

ABSTRACT

Bovine lactic acidosis syndrome is associated with large increases of lactic acid in the rumen, which result from diets that are high in ruminally available carbohydrates, or forage that is low in effective fiber, or both. The syndrome involves two separate anatomical areas, the gastrointestinal tract and body fluids, and is related to the rate and extent of lactic acid production, utilization, and absorption. Clinical manifestations range from loss of appetite to death. Lactic acid accumulates in the rumen when the bacteria that synthesize lactic acid outnumber those that utilize lactic acid. The systemic impact of acidosis may have several physiological implications, including laminitis, a diffuse aseptic inflammation of the laminae (corium). Although a nutritional basis for the disease exists, etiology includes a multitude of interactive factors, such as metabolic and digestive disorders, postpartum stress, and localized trauma, which lead to the release of vasoactive substances that trigger mechanisms that cause degenerative changes in the foot. The severity of laminitis is related to the frequency, intensity, and duration of systemic acidotic insults on the mechanisms responsible for the release of vasoactive substance. The critical link between acidosis and laminitis appears to be associated with a persistent hypoperfusion, which results in ischemia in the digit. Management of acidosis is critical in preventing laminitis. High producing dairy herds attempting to maximize energy intake are continually confronted with subclinical acidosis and laminitis. Management of feeding and husbandry practices can be implemented to reduce incidence of disease.

(**Key words**: acidosis, rumen, carbohydrate, laminitis)

Abbreviation key: **AV** arterial-venous difference, **eNDF** = effective NDF.

INTRODUCTION

Several reviews (26, 59, 61, 120) have described the process of acidosis in livestock and dairy cattle. Carbohydrates with high ruminal availability apparently cause the initial ruminal insult. The severity of acidosis is related to the frequency and duration of diet alteration. Researchers (45, 56, 85) have induced acute or subacute acidosis by repeated doses of highly available carbohydrate. The critical pH threshold of the rumen is <5.0 during acute acidosis and is <5.5 during subclinical acidosis (85). As highly fermentable carbohydrate is introduced to the diet, ruminal VFA production actually increases as pH starts to decrease. Harmon et al. (56) showed that intraruminal dosing with glucose decreased pH to <4.5 within 14 h postdosing. The ruminal microbial profile also changes; *Streptococcus bovis* and lactic acid production both increase. There is a concomitant decrease in *Megasphera elsdenii* and *Selenomonas ruminantium*, and microorganisms that synthesize lactic acid outnumber those that utilize lactic acid (114, 123). As pH continues to drop, growth of *S. bovis* is also impeded; however, lactobacilli fill this niche and continue to produce lactic acid as pH drops. Thus, a spiraling effect is initiated (115).

Ruminal changes initiate several systemic changes. Increased organic acid, particularly lactic acid, and reduced pH result in decreased ruminal motility, stasis, ruminitis, and hyperkeratosis (33, 93). These changes establish conditions for penetration of certain bacteria (*Fusobacterium necrophorum*) through the ruminal wall into the liver where abscesses are established. Other events, which happen simultaneously, are associated with increased ruminal osmotic pressure, decreased extracellular volume resulting in dehydration, decreased cardiac output, decreased peripheral perfusion, decreased renal blood flow, shock, and death (61).

In many dairy operations, the challenge is not acute acidosis, but rather subclinical acidosis, whereby very little accumulation of lactic acid is detected in the rumen; however, pH decreases. Daily episodes of pH <5.5 for given periods ultimately predispose cattle to low grade, subclinical acidosis. Symptoms include erratic appetite, body weight loss, diarrhea, and lameness (45, 99).

Received June 26, 1995.
Accepted December 10, 1996.
[1]Present address: Spruce Haven Research Center, Union Springs, NY 13160.

Laminitis occurs in acute, subclinical, and chronic forms (13, 53, 72, 100). The link between acidosis and laminitis appears to be associated with altered hemodynamics of the peripheral microvasculature (15). Various theories have developed to explain events that occur in the pathogenesis of laminitis. Vasoactive substances (histamine and endotoxins) are released during the decline of ruminal pH and as the result of bacteriolysis and tissue degradation. These substances cause vasoconstriction and dilation, which ultimately destroy the microvasculature of the corium (17, 82). Ischemia results, which causes a reduction in oxygen and nutrients reaching the extremities of the corium. Ischemia causes physical degradation of junctures between tissues that are structurally critical for locomotion (15). The insidious rotation of the distal phalanx (pedal bone) can result in permanent anatomical damage. Manifestations of subclinical laminitis are sole hemorrhages and yellowish discoloration (13, 102). Other clinical manifestations include double soles, heel erosion, dorsal wall concavity, and ridging of the dorsal wall (102).

A challenge for the dairy producer is to identify occurrence of subclinical acidosis and laminitis and to make the appropriate adjustments in feeding and management practices. Acidosis and laminitis can be controlled by increasing the level and type of dietary fiber. To maximize energy intake, a proper balance of nonstructural and structural carbohydrate must be provided, and the amount of effective fiber must be sufficient to promote normal rumen function.

The objective of this review is 1) to characterize incidence, cause, and mechanistic development of acidosis and laminitis, 2) to identify predisposing factors of acidosis to laminitis, and 3) to present preventive management practices that control these metabolic diseases.

ACIDOSIS

Acidosis is caused by the ingestion of greater than normal quantities of ruminally fermentable carbohydrates. The clinical symptoms of carbohydrate overload vary, depending upon the types and amounts of carbohydrates consumed. As a result of carbohydrate overload, acids outside physiologically possible limits are produced and pH is concomitantly reduced, which overwhelms the ruminal and host system. The cascade effects of acidosis originating from the initial ingestion of carbohydrate depend upon the intensity and duration of the insult. Most critical is the pH threshold, which not only relates to microbial growth rates and shifts in ruminal populations but also significantly influences the systemic metabolic state and the ability to catabolize or excrete certain metabolites.

Incidence

Grohn and Bruss (54) evaluated the incidence of ruminal acidosis in >61,000 Finnish Ayrshire cows, which indicated that lactational incidence was only 0.3% of animals affected. However, no details were given regarding the severity of acidosis or diagnostic method used to determine acidosis. The incidence of acidosis is highest during the 1st mo postcalving and relatively nonexistent within 3 mo (54). Onset of acidosis is associated with adaptation to high concentrate diets containing more highly fermentable carbohydrate than cows are accustomed to utilizing during the dry period. Also, the high incidence reflects the inability of the system to handle acid overloads during early lactation.

Acute Acidosis

Acute acidosis results in very sick cows: physiological functions may be significantly impaired and death may occur. Acute acidosis is characterized by a dramatic reduction in ruminal pH ($\leq$5.0), a large increase in lactic acid concentration, an increase in volatile fatty acid concentration, and a large decrease in total protozoa (86). Huntington and Britton (62) demonstrated a 100-fold increase in ruminal concentrations of lactic acid of lambs within 48 h of consuming a diet of 90% concentrate. By 30 h, blood pH decreased from 7.44 to 7.20, packed cell volume increased, bicarbonate and calcium decreased, and lactate increased 6-fold, of which two-thirds was D-lactic acid.

Figure 1 illustrates the developmental and spiraling process (115) of lactic acidosis to a systemic and metabolic state. If the carbohydrate insult persists, the spiraling effect also persists, and irreversible metabolic acidosis in inevitable.

During acute acidosis, blood flow to the gastrointestinal tract is decreased, thereby reducing the absorption of organic acids from the rumen (58). Prolonged exposure of the ruminal epithelium to high acid concentrations can result in hyperkeratosis and parakeratosis, which reduce the absorptive capacity of organic acids, further decreasing pH (96). Although all organic acids accumulate in the rumen, lactate remains the predominant and strongest acid (114). Furthermore, the production and metabolism of D-lactate becomes limiting in the development of

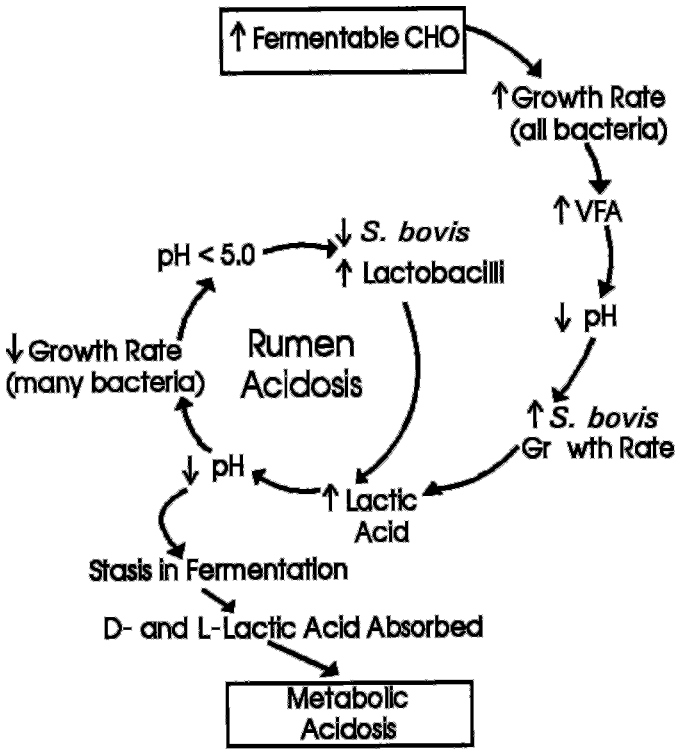

Figure 1. Sequence of events associated with the induction of acute ruminal lactic acidosis. CHO = Carbohydrate.

acute acidosis because D-lactate metabolizes more slowly than L-lactate (47).

Options to Reduce Lactic Acid in the Rumen

A generally accepted concept for ruminal lactic acid accumulation is that lactate producers outnumber utilizing bacteria (114). Critical to this imbalance is pH optimization for growth. Russell et al. (116) illustrated that growth rate of *S. bovis* (a major lactic acid producer) declines dramatically between pH 5.3 and 5.1. Also, *M. elsdenii*, a lactate utilizer, has a reduced growth rate from pH 6 to 5.5. This differential results in significant accumulation of lactic acid when readily fermentable carbohydrate is provided. When ruminal pH is maintained >5.5, equilibrium exists between producers and utilizers, such that lactic acid does not accumulate.

Increased Lactate Accumulation

The primary ruminal microorganisms utilizing lactic acid are *Propionibacterium shermanii*, *M. elsdenii*, and *S. ruminantium*. Hession and Kung (57) investigated the effects of *P. shermanii* and *M. elsdenii* on ruminal fermentation. Treatments were as follows: 10^8 cfu of *P. shermanii*/ml of culture, 10^6 cfu of *M. elsdenii*/ml, and 10^7 cfu of *M. elsdenii*/ml. After approximately 5 h of incubation, pH of the untreated culture was similar to that of *P. shermanii* and, for 10^7 cfu of *M. elsdenii*, was 0.5 pH units greater than the control. Lactic acid concentrations were >30 m*M* for untreated and *P. shermanii* cultures. The *M. elsdenii* cultures remained <3 m*M* throughout fermentation, suggesting that *M. elsdenii* at 10^7 cfu/ml was as effective in elevating ruminal pH and maintaining lower lactic acid concentration as was *P. shermanii* or *M. elsdenii* at lower concentrations.

Nisbet and Martin (89) evaluated the effect of pH on rate of L-lactate uptake in the presence of malate by *S. ruminantium*. Malate substantially increased lactate uptake at every pH tested. There was no effect of lactate uptake in the presence of 10 m*M* glucose, maltose, xylose, sucrose, or D-lactate. Nisbet and Martin (89) indicated that stabilization of ruminal pH through the use of an organic feed additive, such as L-malate, might aid in the prevention of lactic acidosis.

Megasphera elsdenii utilizes 60 to 80% of the lactate fermented in the rumen of cattle (25) and accounts for 20% of the lactate utilizers in the rumen of animals fed high concentrate diets (72). Kung and Hession (69) examined the effect of adding two levels of *M. elsdenii* on pH, lactate, and VFA concentration to in vitro batch cultures. Both the low (8.7×10^5 cfu/ml) and high (8.7×10^6 cfu/ml) *M. elsdenii* levels sustained culture pH at approximately 0.7 pH units higher than that of controls. Both levels were more effective in utilizing D- and L-lactic acids than was the control. However, for the treatment with low *M. elsdenii*, both D- and L-lactic acid spiked at about 5 h of fermentation and then diminished within 2 h. Cultures that were inoculated with *M. elsdenii* had lower acetate and propionate concentrations than did controls. *Megasphera elsdenii* could be effective in reducing lactic acid accumulation in the rumen by lessening the time for adaptation to high concentrate diets.

Robinson et al. (109) induced acute acidosis in steers that were fed a restricted amount of a 50% concentrate diet. On average, *M. elsdenii* prevented acute acidosis (pH >5.0) and increased feed intake (24% more DM) following the dietary switch. These data suggest that *M. elsdenii* can accelerate ruminal adaptation from forage to grain. The implications of this type of product in dairy cattle could be significant because it relates to the transition period and adaptation of high grain levels in early lactation.

As previously mentioned, a major contributory factor to acute acidosis is a greater number of lactic acid producers compared with utilizers. Russell (114) in-

dicated that *S. bovis* and *M. elsdenii* underwent considerable competition. *Megasphera elsdenii* cannot use starch, but *S. bovis* can ferment starch and produce maltose. Both microbes can use maltose; therefore, both also compete for the substrate, and factors affecting the relative numbers of *S. bovis* and *M. elsdenii* are associated with their relative capacity to use maltose, production of lactic acid by *S. bovis*, the use of lactate by *M. elsdenii*, the efficiency of substrate use for growth by both microorganisms, and the tolerance to low ruminal pH (116). These factors can all contribute to a shift in population, which can trigger or sustain ruminal lactic acidosis.

Systemic Lactic Acid Metabolism

Once the physiological conditions in the rumen have overwhelmed the microbial population to sequester lactic acid, absorption into the blood stream and systemic acidosis result. Huber (59) indicated that lactic acidosis is compartmentalized between the gastrointestinal tract and systemic body fluids. Some physiological effects include pH ~5.0 in ruminal digesta and a decrease in the amplitude and frequency of ruminal contractions. A possible mechanism involves duodenal hydrogen receptors, which effectively release secretin and, in turn, inhibit motor activities of the forestomach, ultimately reducing motility (19). Stasis may be beneficial because motility is required to mix bacteria with substrate, which is necessary for absorption (59).

Ruminal contents become hypertonic in relationship to plasma in acidotic ruminants (36, 58, 124). A key regulatory method associated with the maintenance of systemic pH is the bicarbonate buffering system if entry of lactic acid into body fluids is not overwhelming. The bicarbonate buffering system is usually able to maintain pH within critical limits until the acidotic process has run its course.

L-Lactate Turnover

Between 40 to 65% of L-lactate is derived from glucose (107, 108). Approximately 20% of the lactate that enters the system is converted to glucose, and 30 to 50% is oxidized to CO_2. Conversion of lactate to glucose via the Cori cycle represents 5 to 10% of glucose (4, 108, 138). L-Lactate is important as a precursor for fatty acid synthesis as well as glucogenesis. Approximately 16 to 38% of the acetate used for fatty acid synthesis originates from lactate (47). This conversion is particularly important at high intakes during which the turnover rate of lactate is much more rapid than that of acetate (47).

D-Lactate Acid Metabolism

Engorgement of rapidly fermentable carbohydrates initiates a very rapid elevation of both D- and L-lactic acids within 8 h, peaking at 20 h (56). Giesecke and Stangassinger (47) reported that infusion of sugar into the rumen elevated both isomers within 15 to 20 min. The relative proportions of D- and L-lactic acid change as pH decreases. Normally, D-lactic acid constitutes approximately 20% of the total lactic acid concentration at pH 6, which elevates to about 50% at pH <5; concentrations can be as high as 100 to 150 mmol/L (47).

Shifts in ratios of L-lactic acid to D-lactic acid are largely because of a decline in ruminal concentration of L-lactate (56). Harmon et al. (56) evaluated the net portal absorption of lactate in steers that were ruminally infused with glucose or fed a 70% concentrate diet for ad libitum consumption to mimic acute and subclinical acidosis, respectively. Ruminal pH declined to 4.2 by 18 h and to 6.0 by 14 h for cows receiving glucose and concentrate, respectively. Ruminal L-lactate and D-lactate concentrations averaged 53 and 30.2 m*M* for glucose and 2.1 and 1.2 m*M* for concentrate, respectively. Net portal absorption of L- and D-lactate averaged 96.6 and 10.5 for concentrate and 164.5 and 71.8 mmol/h for glucose, respectively. Animals that were acutely acidotic experienced a 6-fold increase in D-lactate absorption, and L-lactate absorption increased 70%, despite higher rumen concentrations. Even though absorption rate increased greatly, the increase had little effect on the relative increases in D- and in L-lactate in arterial and portal blood.

Elimination of D-Lactate

Under normal conditions, removal of D-lactate by oxidation, gluconeogenesis, and renal excretion accounts for 45, 14, and 13% of the total elimination, respectively (47). At higher rates of D-lactate entry into the system, oxidation decreases, and renal excretion is enhanced. The kidney threshold for D-lactate concentration is about 50% of that for L-lactate. Lower absorption rates of D-lactate than of L-lactate favor faster excretion of D-lactate; the reason for the difference is unknown (47). The D-lactate concentrations in blood need to reach 4.25 m*M* before urinary excretion increases in the cow (119). Harmon et al. (55) demonstrated that most D-lactate elimination in cattle was by oxidation (97%), and very little was excreted in the urine, although the relative contribution of D-lactate to total oxidative metabolism accounted for only 0.014% of the total CO_2 expired.

Cattle apparently underwent dynamic changes very rapidly to alter their metabolism to accommodate D-lactate.

Metabolism of D-Lactate

Limitations of D-lactate compared with L-lactate metabolism relate to the presence or absence of specific enzymes and their location within the cell. The lactate dehydrogenase for L-lactic acid is located in the cytosol. The enzyme responsible for D-lactate oxidation is D-2-hydroxy acid dehydrogenase, which is located in the mitochondria. Therefore, the major contrast between the metabolism of the two isomers is that L-lactate can be rapidly oxidized to pyruvate, which can readily translocate the mitochondrial membrane for further metabolism. However, D-lactate must first translocate the mitochondrial membrane to be oxidized. Another challenge is that D-2-hydroxy acid dehydrogenase is inhibited by increased concentrations of pyruvate and oxaloacetate. With high levels of L-lactate compared with D-lactate, conversion of pyruvate to oxaloacetate is rapid. The inhibition of D-2-hydroxy acid dehydrogenase by these metabolites decreases the relative amount of D-lactate that is removed via oxidation and subsequently gluconeogenesis (47).

Under typical acidotic conditions, the primary route of D-lactate elimination and the efficiency of its removal is associated with entry rate. At high entry rates (>45 mmol/h per kg) (75), oxidation to CO_2 decreases, and most elimination occurs by renal excretion. However, under conditions of high gastrointestinal lactate (i.e., acute acidosis), shifts in body water to the gastrointestinal tract reduce urine output, thereby leaving oxidation and gluconeogenesis as the major routes for D-lactate elimination (47).

SUBCLINICAL ACIDOSIS

Acute acidosis presents specific signs and symptoms, which, if caught in time, can be treated directly. Symptoms of subclinical acidosis are insidious and considerably less overt. Often, subclinical acidosis is dismissed as other problems, such as poor forage quality or poor bunk management. Therefore, acidosis can cause a tremendous economic loss, draining productive efficiency potential from dairy herds. The major clinical manifestation of subclinical acidosis is reduced or inconsistent feed intake. Other associated indications include decreased efficiency of milk production, reduced fat test, poor body condition despite adequate energy intake, high culling rate, unexplained diarrhea, and episodes of laminitis.

Subclinical acidosis is a consequence of maximizing energy intake, which requires provision of appropriate levels of physical and chemical dietary components. Often, subclinical acidosis is found in well-managed, high producing herds.

Fate of Ruminal Mucosa in Subclinical Acidosis

Ruminal mucosa is the first major metabolically active tissue to which end products of fermentation are exposed. Mucosal tissue has the tremendous ability to transport or metabolize organic acids that have been derived from ruminal fermentation. The physical form and energy content of the ration has a profound effect on mucosal development (18, 93, 135). Greater mucosal mass is present when diets are predominantly concentrate, suggesting a greater capacity for metabolism and absorption by the ruminal wall; however, enzymatic activities do not appear to change (95, 134, 135). The increased mucosal weight stimulated by increased starchy diets may result in a thickening of the stratum corneum, resulting in a physical barrier for VFA to metabolically active sites and, in fact, may inhibit transport and metabolism within the mucosal membrane (95).

Dirksen et al. (34) indicated that adaptation of the ruminal mucosal is a critical factor in pH stabilization with high sugar or high starch diets. In addition, proliferation status of ruminal mucosa had a greater influence on energy supply to the high producing cow during peak lactation. To maximize pH stabilization and energy utilization, proliferation of the mucosal epithelium should be established and perhaps maximized by the time the animal has calved (34).

Leibich et al. (70) compared two groups of cows during both the prepartum and postpartum periods for changes in ruminal mucosa that were dependent on feed. One group of cows received a low energy diet until 14 d before calving and then was switched to a lactation diet. The other group of cows received the same low energy diet until calving and then was switched to a lactation diet. Prior to treatment, the ruminal mucosal mass of cows in both groups continually declined after the transition to the dry period ration. The mucosal degeneration continued in the group of cows that were not switched to a lactation ration prior to calving, but cows that were switched to a lactation ration 14 d prepartum exhibited a proliferation of the ruminal mucosa after the dietary change. By 8 wk postpartum, both groups had patterns of mucosal development that surpassed the initial level at the end of lactation. A major question remains as to whether mucosal changes ultimately affect the occurrence of postpartum disease or production performance.

Nocek et al. (94) fed diets consisting of 60% concentrate with hay (ground or chopped) or 100% concentrate to Holstein calves from 8 to 20 wk of age. Biopsies of ruminal tissue were obtained at 8 and 20 wk of age for VFA transport and morphological comparisons. Acetate transport across the ruminal epithelium increased between 8 and 20 wk for calves fed hay, but not for calves fed concentrate diets. Propionate transport was highest for calves fed ground hay and lowest for calves fed 100% concentrate at 20 wk of age. No differences in lactate production in ruminal tissue occurred. Morphology of papillae of calves fed 100% concentrate ranged from clumped to long, flat papillary shapes. Lesions were frequently visible at the distal tips. Mucosal folding was common, and clumping of papillae with imbedded hair was evident in the anterior ventral region. Estimated surface area of absorptive mucosa was approximately halved for calves fed concentrate compared with that of calves with 40% ground or chopped hay. Calves fed the 100% concentrate diet had a slightly lower DMI than did calves fed ground hay (2.49 vs. 2.74 kg/d), and daily gains were slightly greater (0.80 vs. 0.73 kg/d) (27). Mean ruminal pH was lower (pH 5.6 to 6.7) for calves fed concentrate (96). During the 12-wk period, high concentrate diets caused no clinical health or performance problems; however, the period was short.

Nocek and Kessler (95) reported morphological abnormalities for calves fed a complete calf ration in contrast to those for calves fed a traditional diet based on hay and grain. After calves were returned to a traditional diet, papillary rejuvenation and development appeared to be normal for calves that were fed the complete calf ration within a 4-wk period. Dirksen (33) indicated that approximately 4 to 5 wk were needed to achieve a highly stable state for the ruminal mucosa after a dietary change from a low to high energy density. A major question that remains is the threshold of ruminal pH or physical form that affects the ruminal mucosa positively enough to allow adequate proliferation for maximal absorption and metabolism and still not be symptomatically hyperparakeratotic, thus reducing metabolic activity and ability of organic acids to be transported. During early lactation, cows are typically fed a diet consisting of primarily acidic silages with ≥ 60% grain. This dietary scenario would appear to be conducive to causing a slow, insidious reduction of absorptive capability in ruminal mucosa, especially when animals were maintained on a wet silage diet for the entire lactation cycle. The regulation potential of ruminal mucosa would probably be jeopardized.

Profile of Subclinical Acidosis

Specific parameters need to be identified relating either to cow manifestations (milk, urine, blood, and feces) or dietary characteristics that would aid in the diagnosis or prediction of predisposition to the disease. Often, bulk tank testing for fat is utilized to identify the onset of subclinical acidosis. Individual acidotic cows demonstrate very low milk fat concentrations that are not necessarily reflected in the overall tank test or mean for that group.

Italian researchers (45) studied the effect of nutritionally induced acidosis on milk composition. At 15, 45, and 90 d postpartum, acidotic cows had less milk fat (2.73 vs. 3.88%) and total milk protein content than did controls. The reduction in milk lipids was related to ruminal inversion of the molar ratio of acetate to propionate. Casein and the ratio of casein to protein tended to decrease, and the ratio of NPN to protein tended to increase, for acidotic cows compared with those of control cows at each time period (Table 1). Also, milk alterations occurred with irregular appetite, transient episodes of diarrhea, and weight loss; no clinical mammary gland alterations were noticed.

Kostyra et al. (68) studied changes in N components in milk after inducing acidosis with sucrose administration. After 24 h of acute metabolic acidosis, the concentration of total N, casein N, N of whey proteins, and NPN increased in milk. Between 48 and 72 h after sucrose administration, a quantitative change occurred in N compounds, but concentrations returned to preacidosis levels by 6 d.

Intake as an Indicator of Subclinical Acidosis

For beef cattle, intake patterns are the most important indicator of subclinical acidosis (120). Fulton et al. (42) evaluated the effect of increased concentrate from 35 to 90% for cattle fed either dry-rolled corn or hard red winter wheat. Intake profiles for cattle that were fed corn appeared to be consistent, indicating that those cattle were adjusting normally to high concentrate diets. However, cattle that were fed wheat diets did not demonstrate increased intake. Evaluation of daily intake data revealed considerable variation in intake patterns across both groups, but the variation was not as great for the cattle consuming corn until the 90% concentrate level was reached, at which time intake decreased dramatically. The cattle that were fed wheat experienced acidosis, reduced their intake dramatically for a few days, recovered, ate again, but were unable to adjust to the wheat. These data would suggest that mean intakes can be very misleading values. Extreme variation in

TABLE 1. Milk protein profile of cows induced with nutritional acidosis.[1,2]

Variable	Time postpartum	Control	Acidotic
	(d)		
Protein, %	15	3.92[a]	3.35[b]
	45	3.28[a]	2.90[b]
	90	2.94[a]	2.65[b]
Casein, %	15	3.47	2.33
	45	2.56	2.07
	90	2.32	1.95
Casein protein, mg/ml	15	0.78	0.69
	45	0.75	0.71
	90	0.79	0.73
NPN:Protein	15	0.055	0.220
	45	0.063	0.070
	90	0.058	0.071

[a,b]Means within a column followed by no common superscript differ ($P < 0.05$).

[1]Gentile et al.(45).

[2]Acidotic state diet is defined as 15 d prepartum to 90 d postpartum: blood pH of 7.3, urine pH of 6.4, irregular appetite, diarrhea, and weight loss.

ruminal pH is sufficient to throw cattle off feed. Cattle that were fed wheat were able to reduce their ruminal acid load by slowing eating rate. Cattle began eating again when ruminal pH reached ≥5.6. Fulton et al. (43) showed that, when ruminal pH was manually adjusted to ≥5.6, for cows that consumed wheat diet, intake patterns were more similar to those of cattle fed corn. For beef cattle, ruminal pH should be maintained at ≥5.6 to minimize the intake depression that is associated with subclinical acidosis; however, no information is available for dairy cows that identifies which pH thresholds are associated with subtle reduction or variation of intake.

Diagnosis of Subclinical Ruminal Acidosis: Predicting Ruminal pH

The identification of specific ration parameters for prediction of ruminal pH would assist in the development of rations that may control the occurrence of subclinical acidosis. R. E. Pitt, J. S. Van Kessel, D. G. Fox, A. N. Pell, M. C. Barry, and P. J. Van Soest (1995, unpublished data) utilized the Cornell Net Carbohydrate Protein Model (8) to predict ruminal pH from a variety of ration nutrient parameters. The model considered the effect of pH on microbial growth and yield as well as products of carbohydrate fermentation, lactate metabolism, concentration and absorption of VFA and lactate in the rumen, intake, production, ruminal volume, and liquid rate of passage. Reported mean pH were correlated to measurements for dietary rations of various species (dairy cows, sheep, and steers). The empirical relationship between ruminal pH and total forage in the dietary DM was poor ($R^2 = 0.15$). Total ration NDF only accounted for approximately 30% of the variation associated with ruminal pH ($R^2 = 0.30$). A factor that accounted for the most variation associated with predicting ruminal pH was effective NDF (**eNDF**) as a percentage of DMI ($R^2 = 0.52$). The measurement of eNDF used was listed by Barry et al. (8).

To evaluate the effect of ration NDF (8) on mean ruminal pH of rations for lactating dairy cows, 27 studies (1, 5, 20, 21, 24, 30, 31, 40, 41, 44, 46, 49, 50, 60, 63, 67, 80, 86, 101, 110, 118, 121, 122, 129, 130, 132, 133, 134) were used to determine the effect of ration NDF on mean ruminal pH. The eNDF values were obtained from data of Barry et al. (8). The eNDF values only accounted for about 5.0% of the variation that was associated with mean ruminal pH. This relationship does not agree with results of other studies (Pitt et al., 1995, unpublished data). The discrepancy could be associated with difference in animal species and thus a wide range of values used in regressions, lack of validity of mean pH, and the method of effective fiber determination.

Ruminal pH as a Diagnostic Tool to Detect Subclinical Acidosis

Subclinical acidosis is a temporarily altered state of the rumen that causes some aberration in fermentation patterns and decreased ruminal pH; however, intensity and duration are not sufficient to cause immediate or overt clinical signs. Therefore, subclinical acidosis should be considered a differential diagnosis associated with a variety of symptoms, including those listed previously. However, nutritional alterations (i.e., adequate effective fiber, alteration of ratios of forage to concentrate, and feeding strategies) influence ruminal pH, which also can affect the occurrence of subclinical acidosis. The only diagnostic test for subclinical acidosis is ruminal pH.

Stomach tubing has been used to collect samples of ruminal fluid for pH determination, but this procedure often has been falsely interpreted because of saliva contamination. Ruminal cannulation is the preferred method of obtaining representative samples of ruminal fluid. Although cannulation has traditionally been limited to research purposes, dairy field professionals are beginning to realize its value and application.

Nordlund and Garrett (100) discuss rumenocentesis or percutaneous needle aspiration as a means of collecting ruminal fluid for diagnosis of subclinical acidosis. I evaluated rumenocentesis with the following objectives: to determine whether one ruminal lo-

cation would yield a representative ruminal pH and to determine the time of sampling in relation to feeding to achieve nadir (J. E. Nocek, 1995, unpublished data). The study was a 3 × 3 Latin square with three forage to concentrate ratios: 30:70, 40:60, and 50:50. Three ruminally cannulated cows were utilized, and ruminal samples were taken at hourly intervals twice prior to feeding, at 7 h postfeeding, and at 12 h postfeeding (one sample). Sample locations were as follows: 1) composite of six locations by aspiration (about 200 ml), 2) one location for aspiration of the ventral rumen (50 ml), and 3) one point for percutaneous needle aspiration (about 5 ml) in the same location as the aspiration of the ventral rumen. This location would be the same as that recommended for sampling by rumenocentesis. There were no significant differences between composites of multiple samples and one sample aspiration of the ventral rumen. Samples taken at 1600 h by rumenocentesis were 0.1 to 0.2 pH units higher than the mean values for the composite and single samples. Garrett et al. (44) compared needle rumenocentesis versus cannula collections and found that needle values for the probes were approximately 0.35 units lower than those of samples obtained via ruminal cannula. The following equation related cannula pH and needle probing: cannula pH = 3.257 + 0.506 (needle pH) ($r = 0.73$, $P > 0.01$).

To reach the nadir when the TMR was fed once daily, ruminal samples should be taken 5 to 8 h postfeeding. These recommendations coincide with those of Nordlund and Garrett (100) for feeding a TMR. Cows fed forage and concentrate separately should be sampled 2 to 5 h after concentrate feeding (100). Cows should be selected from high risk groups during the first 60 d postpartum. Because considerable variation is inherent, a minimum of 10 animals per group should be considered. Nordlund and Garrett (100) indicated that, if >30% of the cows within the particular subgroup have a pH of ≤5.5, the group should be considered as abnormal, and further evaluation should be conducted of feeding management practices. When pH values were between 5.6 and 5.8, the group was considered to be marginal. Finally, if all pH were >5.8, the pH status of the group was considered to be normal. These guidelines need to be evaluated further for cows consuming high energy diets (1.72 Mcal/kg) to determine the nadir. This type of diagnostic tool should be used in conjunction with other factors, such as evaluation of ration, management practices, and herd health problems.

Risk of Acidosis

Although guidelines exist for acidosis risk, high producing cows that consume large quantities of grain (55 to 60% of DM) tend to have lower ruminal pH during the day. It is unknown how low pH can go and for how long before negative effects are demonstrated. Nordlund (99) described the onset of acidosis as periparturient cow acidosis and ration formulation and delivery acidosis, which suggest that the different physiological occurrences that normally take place during transition phases of the lactation cycle predispose the cow to acidosis. In addition, management factors regarding ration formulation and delivery can mediate the effect of these physiological states and the risk of contracting acidosis.

In more closely evaluating the transition between physiological states and management practices, there appears to be considerable overlap from the close-up dry period through the peak of DMI. These two major causative regions could be designated as cow-mediated acidosis and management-mediated acidosis, respectively.

Cow-Mediated Acidosis

During the transition from the dry period to lactation, several physiological events and management practices occur. The DMI of grain increases from 30 to 40% to approximately 60% of the ration DM and is maximized at approximately 12 to 14 wk postpartum. Microbial adaptation to ration changes can significantly influence the potential for acidosis development. During the close-up dry period (1 to 3 d prior to calving), a reduction in DMI occurs that can significantly influence the microflora, pH, and endotoxin production in the gastrointestinal tract. Cows are predisposed to metabolic and infectious diseases during the first 30 to 35 d postpartum. Therefore, cow-mediated acidosis is associated with the normal course of events (physiological stress) presented by the cow. If transition events and stress are not managed correctly, some degree of acidosis is likely to occur.

Management-Mediated Acidosis

Cow- and management-mediated acidosis overlap. During the transition period and through 50 d postpartum, management of the cow-mediated events play an important role in the development of acidosis.

Interpretation of the normal ecological balance within the rumen can ultimately assist in predisposing the cow to subacute acidosis. When intake is reduced, energy metabolism of the ruminal microorganisms as well as the host system is interrupted. Intake is controlled by a balance of physical and chemostatic mechanisms. The challenge is to ensure

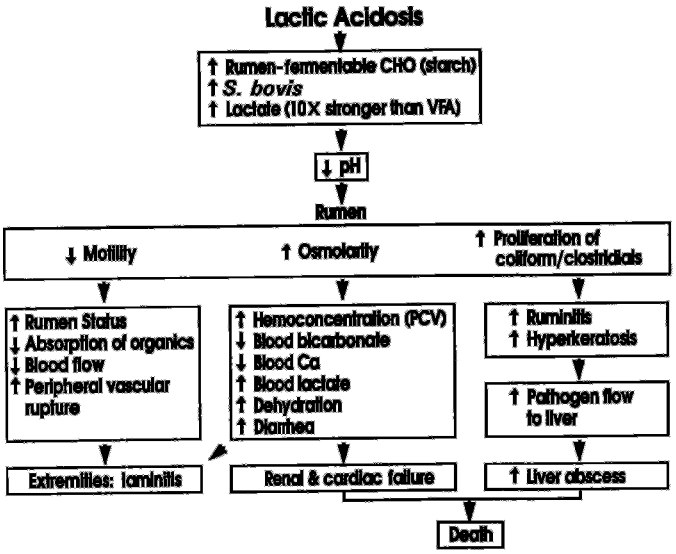

Figure 2. Progression of physiological events that link acidosis with laminitis. CHO = Carbohydrate.

that both mechanisms work in synchrony so that one does not overpower the other (i.e., too much grain or fermentable carbohydrate vs. too much forage).

Factors such as the amount and type of grain, grain processing, and forage type, quality, and levels influence intake patterns, energy metabolism, and subclinical acidosis. The rate and extent of digestion and the amount of starch intake modify the severity of acidosis. Grain mixes containing finely ground or highly processed cereal grains have the fastest rates of ruminal digestion of starch. It is critical that the grain portion of the diet complement the forage type and quality and contain ingredients with various levels of ruminal carbohydrate availability. Both low roughage and reduced particle size exacerbate acidosis during the critical transition period.

Although several factors (e.g., heat, cold facilities, management, and diet composition) influence intake, managers ultimately must anticipate and compensate for intake challenges associated with normal daily practices.

The Implications of Acidosis on the Development of Laminitis

The progression from acidosis to laminitis is associated with several systemic phenomena. Figure 2 outlines several aspects that have been associated with the development of laminitis. A very strategic and critical apex in this entire cascade process is the reduction of ruminal pH. The effects of pH on the pathogenesis of the rumen, liver, and gastrointestinal tract ultimately affect hemodynamics and predispose cows to laminitis. The onset of acute acidosis presents very hastened and dramatic hemodynamic insults that predispose animals to severe but short episodes of acute laminitis. Several severe episodes of short duration or low insidious levels of acid can create a situation that predisposes the rumen to hyperkeratosis, pathogen infiltration, and, ultimately, abscessed liver to variable degrees. In addition, changes in gastrointestinal tract osmolarity, hemoconcentration, and vascular destruction can ultimately result in a low grade but irreversible laminitic process.

LAMINITIS

Definition and Incidence

The scientific name for laminitis is pododermatitis aseptic diffusa, which is an aseptic inflammation of the dermal layers inside the foot. Table 2 illustrates surveys that have been conducted to identify the incidence of lameness in various parts of the world. Across surveys, mean incidence of lameness ranged from 5.5 to 30%. Within surveys, incidence of lameness ranged from 0 to 55%. Very few studies have been conducted or published to evaluate factors affecting lameness in commercial US dairy herds. Wells et al. (136) evaluated the relationship between clinical lameness and risk factors for individual cows in Minnesota and Wisconsin dairy herds and concluded that body weight, body condition score, rear lateral digit angle, nontarsal rear limb superficial swelling, abnormal hoof overgrowth, and limb laceration were prevalent risk factors for clinical lameness. Table 3 illustrates the types and percentages of foot lesions found in the largest survey (115). Approximately 62% of the total of manifested lesions could be associated with laminitis in some form, suggesting the importance of laminitis as a cause of lameness.

To understand the laminitic process as it relates to metabolism and subsequent mechanical and physical damage, the basic anatomical components of the bovine foot must be understood. Fundamental details can be found elsewhere (53, 83, 90).

Causes of Laminitis

Laminitis has a multifactored etiology and is thought to be associated with several, largely interdependent factors (83, 100). Nutritional management has been identified as a key component in the development of laminitis, particularly the feeding of increased fermentable carbohydrate, which results in an acidotic state. Metabolic and digestive disorders

TABLE 2. Incidence of lameness from surveys.

Study	$\bar{X}$	Range	Herds	Location
			(no.)	
Russell et al. (113)	5.5	1.8–11.8	1821	United Kingdom
Eddy and Scott (37)	7.3	0–32	150	United Kingdom
Philipot et al. (104)	8.0	. . .	160	France
Dewes (32)	14.0	. . .	4	New Zealand
Wells et al. (136)	13.7/16.7	. . .	17	United States
Tranter and Morris (127)	16.0	2–38	3	New Zealand
Whitaker et al. (137)	25.0	2–55	185	England, Wales
Prentice and Neal (106)	30.0	. . .	. . .	England

can predispose the cow to laminitis. Hormonal changes associated with parturition and other phases of the lactation cycle can have an impact on certain physiological changes. Infectious diseases, such as mastitis, metritis, and foot rot, can impose specific endotoxic insults (76). Environmental aspects, such as hard surfaces, lack of or little use of bedding, and lack of or excessive exercise on undesirable surfaces, can predispose animals to mechanical damage (13). Other factors, such as body condition, body weight, and feet and leg structure, can unnaturally increase the weight load and stress on feet, exacerbating the internal mechanical damage that is associated with laminitis.

Mechanisms of Laminitis Development

The mechanistic phases of laminitic development can be best described as alternating stages of disturbances relating to metabolic and subsequent mechanical degradation of the internal foot structure (14, 83, 100). The process can be segmented into various phases.

Phase 1

The initial activation phase of laminitis, phase 1, is associated with a systemic metabolic insult (Figure 3). This phase is a result of ruminal and, subsequently, systemic pH. The reduction in systemic pH activates a vasoactive mechanism that increases digital pulse and total blood flow. Depending upon the insult that initiates the process, endotoxins and histamine can be released, which create increased vascular constriction and dilation and, in turn, cause the development of several unphysiological arteriovenous (**AV**) shunts, further increasing blood pressure. The increased blood pressure causes seepage through vessel walls, which ultimately are damaged. Damaged vessels then exude serum, which results in edema, internal hemorrhaging of the solar corium from thrombosis, and ultimately the expansion of the corium, causing severe pain.

Phase 2

As a result of the initial insult, there is mechanical damage, phase 2, which is associated with the vascular system (Figure 3). Once vascular edema has occurred, ischemia (local anemia) results in hypoemia of the local internal digital tissue, causing tissue hypoxia, resulting in fewer nutrients and less oxygen reaching the epidermal cells. Ischemia itself can trigger a further increase in AV shunting. Trauma, stress, and certain actions releasing hormones and chemicals can increase AV shunting. As a result of previous events, increased blood pressure further increases vascular seepage in the lower part of the digit as well as edema and ischemia. This cycle continues as long as the initial insult continues.

TABLE 3. Types and percentages of foot lesions: incidence of laminitis and associated lesions.[1]

Foot lesion[2]	(%)
White line abscess	15.6
Sole ulcer	13.6
Underrun heel	8.7
Aseptic laminitis	5.3
White line separation	4.7
Deep sepsis	3.5
Punctured sole	10.4
Interdigital hyperplasia	4.8
Foreign body in sole	3.5
Interdigital foreign body	2.2
Overgrown sole	2.2
Sandcrack	1.3
Other	7.5
Total	100.0

[1]Russell et al. (113).

[2]First seven lesions listed account for 61.8% of foot lesions.

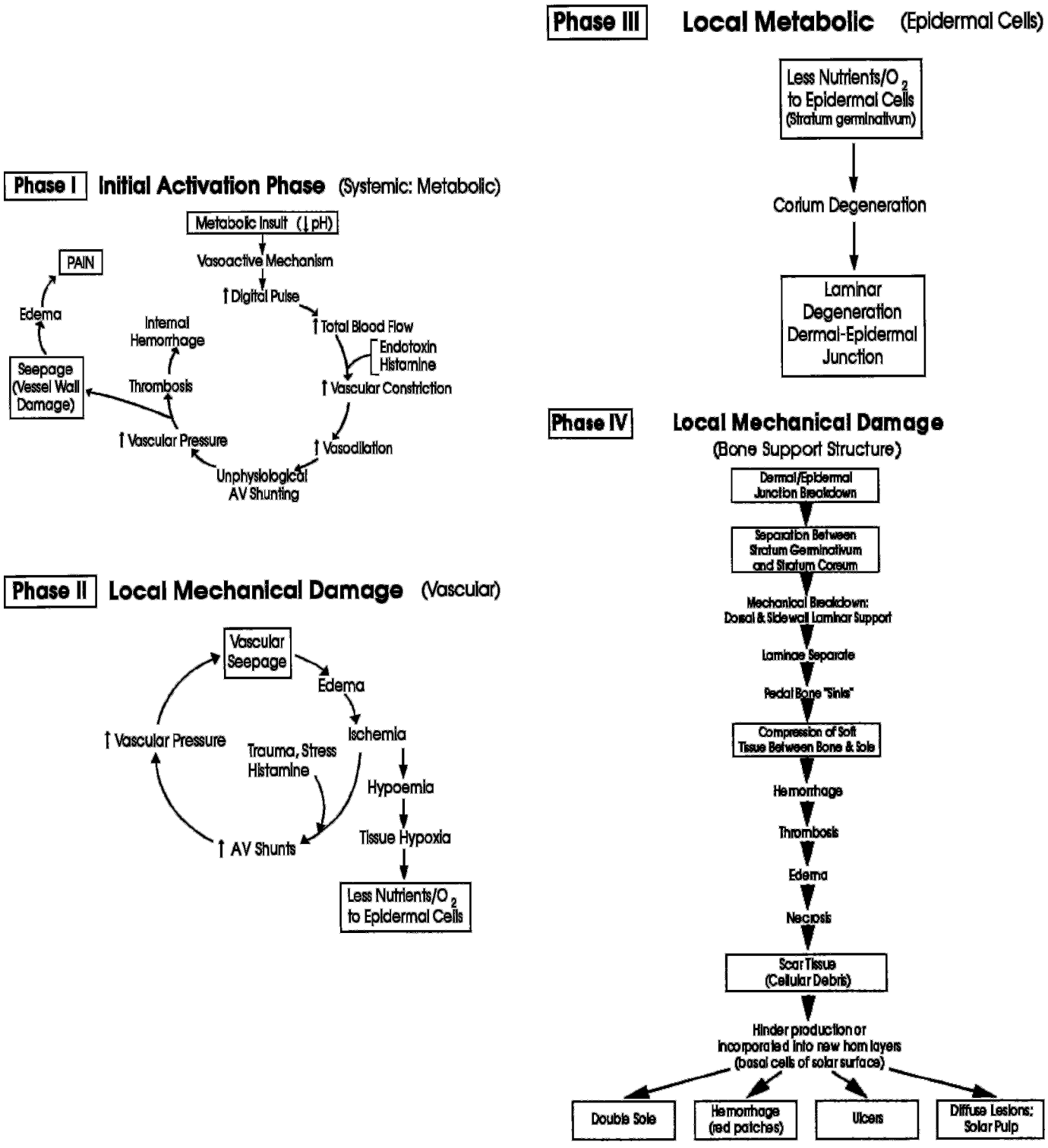

Figure 3. The phasic progression of laminitis development. Phase 1, initial activation; phase 2, local mechanical damage; phase 3, local metabolic insult; and phase 4, progressive local damage of the bone structure. AV = Arteriovenous.

Phase 3

In phase 3, as a result of the mechanical damage associated with microvasculature and fewer nutrients provided to the epidermal cells, the stratum germinativum in the epidermis breaks down (Figure 3). These events ultimately cause corium degeneration and breakdown of the laminar region associated with the dermal-epidermal junction.

Phase 4

Ultimately, in phase 4, local mechanical damage occurs (Figure 3). A situation develops in which the epidermal junction is broken down, which results in the separation of the strata germinativum and corium. This separation in turn results in a breakdown between the dorsal and lateral laminar supports of the hoof tissue. Ultimately, the laminar layer separates, and the pedal bone takes on a different configuration in relationship to its position in the corium and dorsal wall. As the bone shifts in position, it causes a compression of the soft tissue between the bone and sole, which is extremely susceptible to damage. The compression of this soft tissue results in hemorrhage, thrombosis, and further enhancement of edema and ischemia, resulting in a necrotic area within the solar region of the foot. Small areas of scar tissue can accumulate because of the necrotic process. Once this process is triggered, continued potential for tissue degeneration persists because cellular debris is incorporated into the cellular matrix and the production and integrity of new horn tissue layers are hindered. Ultimately, a variety of processes can occur as a result of the incorporation of scar tissue intervention, which includes double sole phenomenon, sole hemorrhages (red blood patches), bruises, diffuse lesions, and solar pulp. Figure 4 depicts the anatomical and physiological aspects associated with development of the various forms of laminitis: acute, subclinical, and chronic (38, 73, 74, 131).

Acute Laminitis

During acute laminitis, the cow is systemically ill. Inflammation of the corium is evident; however, very few if any clinical signs are manifested. The cow is prone to recurrences if the metabolic insults persist. Vessel seepage, edema of the capillary beds, and AV shunting are all initiated. Vascular congestion is present. The major local clinical signs in addition to intense pain include some swelling and temperatures that are slightly warmer than normal above the coronary band in the soft tissue area.

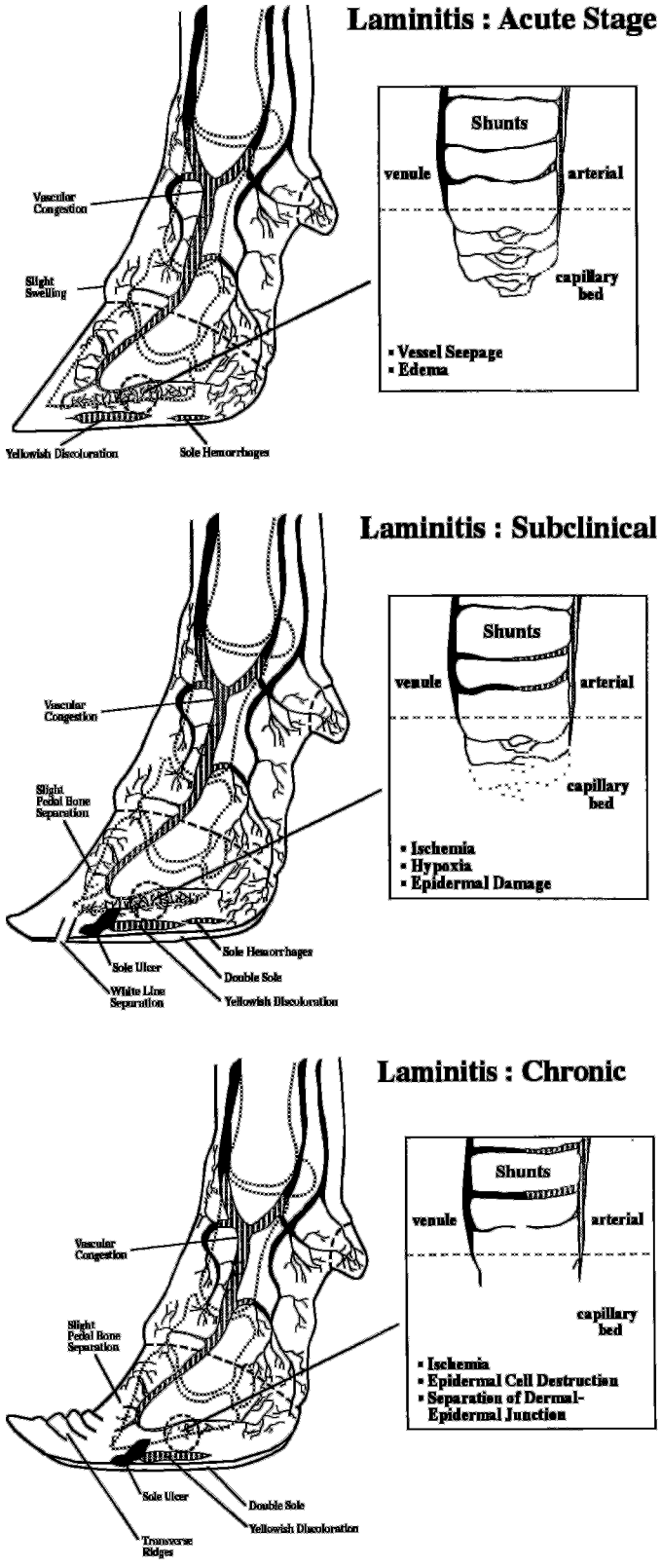

Figure 4. Stages of laminitis development: severe (acute), subclinical, and chronic.

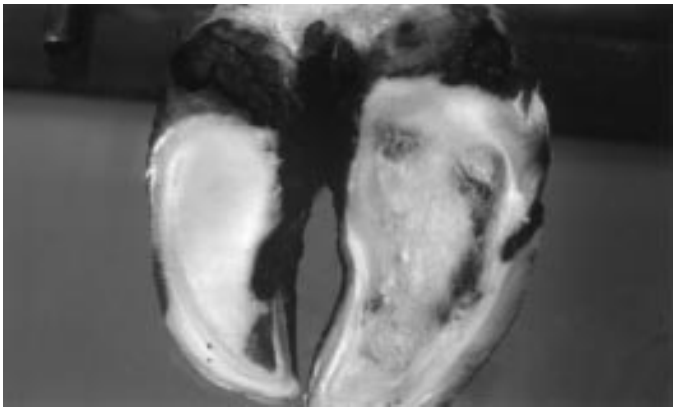

Figure 5. Illustration of the lateral digit of a posterior foot that is broadened, flattened, and possesses elongated sole characteristics of a laminitic digit. Sole hemorrhaging, yellow discoloration, and bruised area are visible in contrast to the medial toe (left).

Subclinical Laminitis

Subclinical laminitis can be a long, slow, insidious process that is dependent upon the persistency of low grade insults. The horn becomes physically softer during this period, and the yellowish coloration of the sole is caused by serum seepage from the vessels into the solar corium. Hemorrhagic stains are manifested in the solar area, particularly in the white line regions, the apex of the sole, and the sole-heel junction. Internally, ischemia, hypoxia, and epidermal damage are key aspects associated with this stage. Arterial-venous shunting becomes an increasing occurrence. White line separations, frequent dorsal wall ridges, and a slight tilting to definite rotation of the pedal bone are characteristic internal manifestations. Sometimes the soles of affected feet are soft and warm but without visible lesions. This appearance may be associated with integral hemorrhagic areas. A possible theory about the development of heel cracks and double soles may be that hemorrhagic areas, once walled off, become a perfect environment for anaerobic bacteria to grow. As gas and exudate develop, they are forced by pressure to points of least resistance, which often are at the junction of the sole and heel bulb.

Chronic Laminitis

During the chronic stages, several changes are associated with the localized area of the digit. The growth pattern of the keratinized horn is disrupted, and the shape of the digit is altered, becoming more elongated, flattened, and broadened (Figure 5). Grooves and ridges on the dorsal wall, giving a rippled appearance, become prominent. Internally, the pedal bone has separated from the dorsal aspect of the wall. Often, ulceration can be demonstrated at the solar region of the foot. Double soles with yellowish discoloration continue to be a major clinical sign. Continued ischemia results in destruction of the capillary beds and development of AV shunts; arteriosclerosis is a prominent histopathological feature. Cellular destruction results in the separation of the dermal-epidermal junction and, ultimately, internal foot destruction. In severe situations, the distal aspect or keel portion of the pedal bone can protrude through the corium and hard-horned tissue of the sole. Figure 6 shows a cow with chronic laminitis. Once the disease process has reached this point, the damage has been done; no therapy can return the foot to a normal configuration. The degree of chronic laminitis depends on the intensity and frequency of each acute episode and, ultimately, the degree of damage each preceding episode has caused as a result of the initial metabolic insult.

PATHOGENESIS OF LAMINITIS

Vasoactive Substances

Destruction of the normal hemodynamic process has been identified as a major etiological factor associated with the development of laminitis (14, 76). Histamine has long been identified as a potent vasodilator and arterial constrictor (22) and is naturally found in tissues and blood. Early works by Dain et al. (29) showed a direct correlation between the pH of the rumen, histamine concentration in the ingesta, and health of the animal. Sanford (117) also indicated a similar relationship between histamine concentration and pH of the ruminal fluid and suggested that histamine formation was a result of a change in microbial population. Histamine can be formed by the decarboxylation of histidine in several lactobacilli species (111).

The hemodynamics that are associated with the circulatory effects of histamine on laminitis coincide with mode of action. Early detection of laminitis and treatment with antihistamine has had good results (64). Maclean (75) indicated that histamine was slightly elevated during acute laminitis of cattle fed diets that are high in concentrate; however, histamine is somewhat higher in the serum of cows in chronic stages of laminitis. Once histamine is absorbed into the portal circulation, it is rapidly methylated or oxidized to various inactive forms (48). Oral administration of histamine has had no effect on causing laminitis because histamine is metabolized by the liver, the gastrointestinal wall, and the intestinal bacteria (48). A more feasible

Figure 6. Illustration of "slipper foot"; concave sole, elongated toe, dorsal wall concavity, and ridging and swelling of the coronary band are characteristic of a chronic laminitic digit.

explanation for the elevation of serum histamine during the occurrence of chronic laminitis might be the release of histamine as the result of the corium tissue breakdown, stress, or protein degradation that is associated with other necrotic diseases such as mastitis and metritis. Dougherty et al. (35) injected sheep with histamine but were not able to reproduce characteristics of lambs dosed with the ruminal contents of acidotic sheep. Anaerobic bacterial growth in developing abscesses and hemorrhagic areas of the foot might also contribute to histamine production.

Acidosis creates ruminal conditions that are appropriate for a chain of events associated with the liberation of *Fusiformis necrophorus.* These bacteria permeate the wall of the rumen as a result of ruminitis or hyperkeratosis and enter the portal circulation, predisposing the cow to liver abscesses. The degeneration process associated with this chain of events can also cause release of histamine. The primary target of endotoxins appears to be vascular arterial tissues, which affects the release of vasoactive mediators, thus inducing an acute inflammation of the dermis and associated vascular responses (51). Endotoxins, released from lysed bacteria as a result of low ruminal pH, have been extracted from ruminal fluid (84).

Controversy also exists about the specific action of histamine and vasoactive substances on the process affecting hemodynamics. Brent (17) indicated that histamine increases capillary permeability and arteriolar dilatation. The *Merck Index* (81) identifies histamine as a potent vasal dilator, and Chavance (22) identified histamine as a potent arterial constrictor. If histamine is an arterial constrictor and vasal dilator, blood pressure and flow would increase to the capillary beds and allow pooling, vessel rupture, serum seepage, and hemorrhaging. If the reverse were the case, then pooling would also occur because of constriction of veins rather than arteries. In any event, the impedance of blood flow and pressure building within the capillaries forces fluid through the vessels into the interstitial tissue spaces setting up ischemia.

When the microvasculature of the corium is affected by vasoactive substances, vascular destruction is inevitable. When blood is not returned to circulation by the musculature of the vascular system, seepage and hemorrhage can result. The anatomical features of the corium vascular network play a very important role in the development of various stages of laminitis (83).

The involvement of histamine and endotoxins fits well with the nutritional theory of laminitis development. However, histamine release can be caused by a variety of factors other than nutritional origin, such as environmental stress, concussion, trauma associated with concrete floors, overcrowding, and infectious diseases, causing tissue breakdown. This process accentuates the dynamics of the etiology of laminitis, particularly because many of these events occur during the first 50 d postpartum (112).

Even though histamine and endotoxins have received much of the attention that is associated with vasoactivity, other substances may be important separately or in conjunction with histamine in creating an altered hemodynamic state. Serotonin is found in the mucus membranes of the intestinal tract and is liberated by blood platelets (81). The specific mode of action can be associated with smooth muscle contraction as well as dilation of capillary beds and contraction of arterioles. Hormonal changes associated with parturition (2) have been associated with vascular dynamics. Estrogen has peripheral dilation activity and also enhances catecholamine-mediated vessel constriction, which could have a significant impact on hemodynamics (2).

Characterization of Laminitis

Philipot et al. (104) conducted a survey to characterize clinical laminitis and to identify risk factors that are associated with affected cows. A total of 4896 cows from 160 French dairy farms were evaluated. Very few (11%) cows were free from foot lesions, and >25% of the cows were affected by at least one of the following lesions: heel erosion, sole hemorrhage, dorsal wall concavity, and yellow sole coloration. Three of the lesions that are associated with laminitis did not cause lameness: yellow discoloration of the sole, brittle horn, and dorsal concavity of the wall. Eighty percent of the cows were lame during the survey, and at least one foot lesion was identified in 89% of the

cows. The relationship between podolesions and laminitis identifies the presence of a subacute and chronic phase. The subacute phase is characterized by yellowish colorization of the sole, white line separation, double soles, and sole ulcers; the chronic phase is characterized by wall ridges and concavity of the dorsal wall. Other researchers (126) have indicated that yellowish colorization is more specific to laminitis because this colorization represents serum exudation from the corium; solar hemorrhaging can be associated with a variety of disorders, including mechanical injury. Subacute laminitis was further categorized into a benign or serious phase. The benign phase did not include lameness, but consisted of

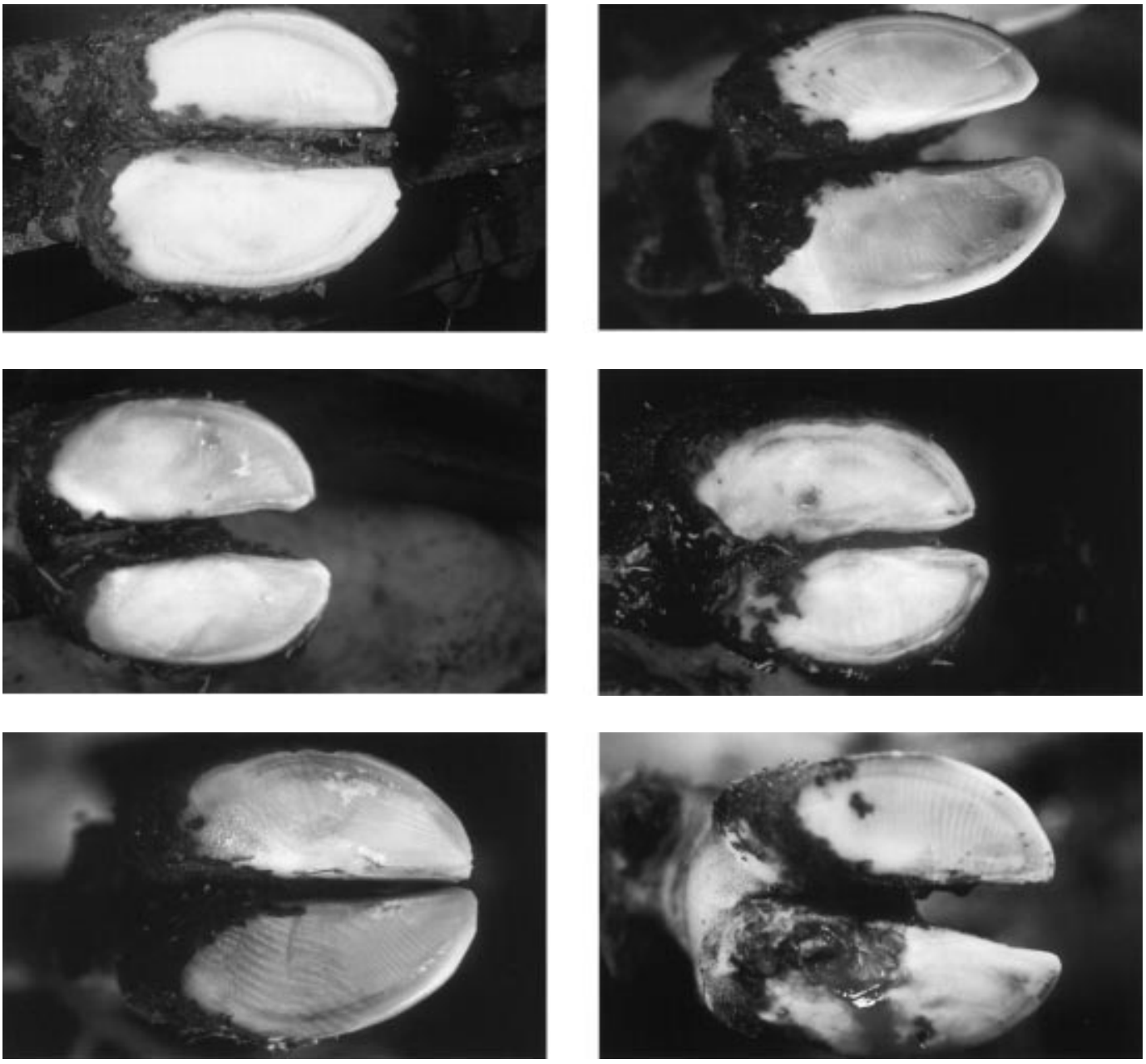

Figure 7. Illustration of various degrees of sole hemorrhaging appearing in order from top to bottom, left to right: 0 = no hemorrhage, 1 = light hemorrhagic permeation in small area (<50% surface), 2 = light hemorrhagic permeation in large area (>50% surface), 3 = dark hemorrhagic permeation in small area (<50% surface), 4 = dark hemorrhagic permeation in large area (>50% surface), and 5 = sole ulceration (at any location:exposed corium).

yellow colorization of the sole. The serious phase was characterized by yellow colorization of the sole plus at least one of the three subacute components of white line separation, double soles, and sole ulcers. Yellow colorization of the sole was a higher risk factor of laminitis than hemorrhaging of the sole (128).

Subclinical Laminitis: Involvement of Sole Hemorrhaging

Sole hemorrhaging is very common and often is related to the incidence of subclinical laminitis. Enevoldsen et al. (39) indicated that 29.7% of first lactation cows and 24.7% of cows in second and third lactations have sole hemorrhages in >1 foot. Other researchers (6, 82, 102, 128) also found a >25% incidence of sole hemorrhaging. Laminitis is associated with inflammation of the local corium, a process that involves vascular breakdown, hemorrhaging, and exudation of the serum from capillary beds. As the horn tissue of the sole grows, the hemorrhaging moves to the external surface, and ultimately, the external tissue of the sole is a prominent clinical sign that internal hemorrhaging has occurred. The interval between occurrence and appearance of a hemorrhagic area is a function of growth rate. Growth rate of the horn is approximately 5 to 6 mm/mo (53, 77). Sole thickness ranges from 10 to 12 mm. Depending upon trimming objectives, the expected time needed for a hemorrhage to externalize is approximately 2 mo.

Bargai and Levin (6) indicated that sole hemorrhaging and white line separation are sequel lesions of subclinical laminitis. Inflammation of the corium results in hemorrhaging, which is a clinical sign of laminitis (11). Hemorrhages of the sole are commonly found 2 to 3 mo postcalving and are very common in first calf heifers (11, 52).

The severity of hemorrhages is related to the intensity and duration of the insult that caused the vascular disruption. Bergsten (12) developed a photometric method of scoring to record sole hemorrhages: 0 = no hemorrhage, 1 = slight hemorrhage in small area, 2 = slight hemorrhage in large area, 3 = moderate hemorrhage in large area, 4 = severe hemorrhage in small area, and 5 = severe hemorrhage in large area or with ulceration. A consistent methodology to evaluate sole hemorrhages is important in characterizing the pathogenesis of laminitis. Evaluation between two assessors for sole hemorrhages indicated good correlation ($r^2 = 0.78$; $P < 0.001$). Figure 7 illustrates various degrees and locations of sole hemorrhaging. The site of sole hemorrhaging or ulceration is a reflection of the severity of the disease process. For example, if sole hemorrhaging was relatively light in intensity but diffuse throughout the entire region of the sole (score 2), vascular damage was neither severe nor associated, in particular, with mechanical damage associated with shifting bone structure at this time. More specific intense hemorrhaging at a specific locus (score 3) would suggest a mechanical degradation associated with pedal bone separation and irritation.

The site of sole necrosis depends on the angle at which the pedal bone descends. If the distal point of the pedal bone descends first, compression and destruction of the corium of the sole can cause hemorrhaging or ulceration. If detachment between the dorsal aspect of the pedal bone and corresponding wall occurs, the distal tip of the bone could eventually cause ulceration in the toe region. Figure 8 depicts a foot with separation of the dorsal aspect of the pedal bone.

Bergsten (13) evaluated 11 laminitic and control herds for 2 consecutive yr. Sole hemorrhages were scored for each digit and were related to clinical laminitis. Herds with a high incidence of laminitis had a greater tendency for lesions than did control herds, and hind digits were affected more than front digits. Primiparous heifers were more prone to sole hemorrhage than were multiparous cows. Primiparous heifers had a higher score, regardless of whether they came from a laminitic or control herd; hind feet were twice as susceptible as front feet for all cows. Higher hemorrhage scores for cows were associated with housing on hard concrete floors with little or no use of bedding. The occurrence of sole hemorrhaging was about 80 to 90% during the 2 yr. Others have also shown a high incidence (16). Sole hemorrhages of the front feet were more prevalent on the medial than the lateral digits; the reverse was true for the hind feet. Other factors that were related

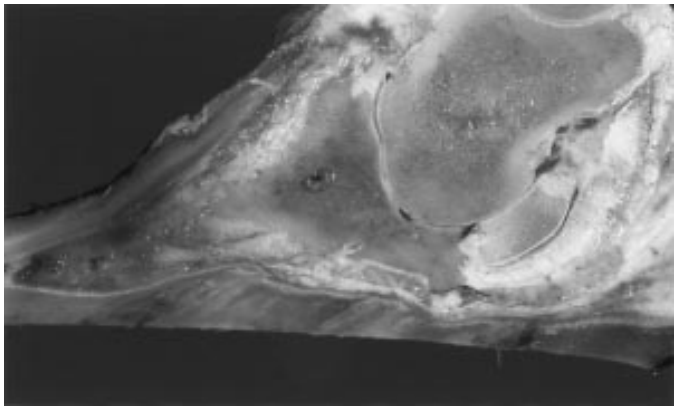

Figure 8. Depicts a cross sectional view of a digit; note the separation of the dorsal aspect of the pedal bone.

to sole hemorrhages were associated with feeding practices, which included fewer than four daily feedings of concentrates, the short time allocated for cows to consume concentrates, and the feeding of concentrates as the first meal in the morning or afternoon (13). The incidence of sole hemorrhages was positively correlated with clinical laminitis, which agreed with results of Livesey and Fleming (71), suggesting that sole hemorrhaging can be used to gain information relating to the etiology of subclinical and clinical laminitis (13).

Greenough and Vermunt (52) showed a distinct pattern of changes in severity of sole hemorrhage with respect to calving and parity. Primiparous heifers demonstrated more severe sole hemorrhaging through calving, and then the incidence decreased dramatically; the incidence and severity tended to increase during the dry period and continued to increase during the postpartum period for multiparous cows. This trend may be associated with recurring episodes of solar hemorrhaging and scar tissue from previous occurrences.

Histology of Bovine Laminitis

Specific vascular changes that were associated with laminitis included dilation of the capillaries and venules, proliferation of the tunica intima, hypertrophy of the tunica media, and fibrosis of the tunic adventitia of arteries and arterioles; arteriosclerosis occurred mainly in the corium (3). Boosman et al. (14) investigated the histopathology of chronic bovine laminitis in 20 rear lateral digits. Five histopathological parameters were used to evaluate digits that had clinical signs of chronic laminitis. Digits with chronic laminitis were no more severely affected with chronic degenerative changes than were digits of cows in the control group. The number of AV shunts increased as age increased. In the digital cushion area, more severe abnormalities occurred with respect to arteriosclerosis, AV shunts, and sole hemorrhages. However, only minor influences of age on laminitis were shown. In addition, no pathological changes, such as thrombosis, which is correlated with laminitis, were evident. Chronic bovine laminitis may be related to the altered hemodynamics in the underlying foot without specific pathological events (14). The study was also characterized by the fact that the 20 specimens were obtained from the slaughterhouse, and the age differential was identified by examining the teeth.

Boosman et al. (15) evaluated the arteriographical and pathological changes associated with chronic laminitis in 76 hind digits that were obtained from the slaughterhouse. Lateral digits clearly had a greater total score for laminitis than did medial digits. Differences between medial and lateral claws were explained by the fact that horn tissue in the lateral digit grew faster because of overburdening. More severe arteriographical lesions (i.e., arterial dilation, tortuous and irregular vascular course, and constriction of vessels at the exit of the pedal bone) were present in lateral than in medial toes. Primary claw arteries were often either dilated or constricted; however, constrictions were particularly prominent in the toe region. The correlation ($P < 0.05$) between the total laminitis score and arterial abnormalities in the claw was positive. This relationship did not change when the score for sole hemorrhages was subtracted from the total laminitis score, suggesting that sole hemorrhaging might not be important in the manifestation of subclinical laminitis. Boosman et al. (15) identified ridges in the dorsal wall as the best criteria to predict the presence of arteriographic lesions because they were more reliable than sole hemorrhaging. Mortensen (83) also agreed with this suggestion. Figure 9 illustrates findings of Boosman et al. (15) on the development of manifestations of chronic clinical laminitis. A subclinical episode of laminitis results in muralthrombosis, which causes arteriosclerosis. Arteriographic lesions can also be influenced by other factors including aging, hypertension, mechanical stress, and hypoxia. These changes can influence pododermal hemodynamic changes, causing loss of vascular integrity, sole hemorrhaging, poor quality horn tissue, and dorsal wall concavity. Therefore, development of chronic laminitis is thought to be associated with continuous hypoperfusion of the digits.

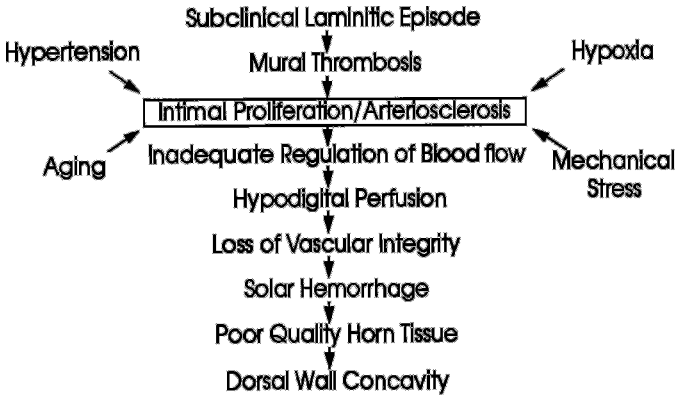

Figure 9. Illustration of the development of the clinical manifestations of chronic laminitis. Adapted from Boosman et al. (15).

Nutrition and Laminitis

Although the etiology of laminitis is multifactorial, nutrition has received considerable recognition as the cause. A major challenge regarding nutrition is a lack of information to specify threshold levels of carbohydrate that initiate nutritional insult (i.e., acidosis). Carbohydrates constitute approximately 70 to 80% of the dairy cow ration; therefore, the level and availability in various rations can have a significant impact on ruminal metabolism.

The amount of feed that is necessary to induce ruminal acidosis depends on the type of carbohydrate processing, the adaptation period, the nutritional status of the cow, and the frequency with which the carbohydrate is fed (42, 86, 91, 92, 93). Nocek and Tamminga (98) show the rate and extent of ruminal digestion of various feedstuffs. Barley, wheat flour, oats, and steam-flaked corn all have ruminal starch availabilities >85%. However, processing (grinding, steam-flaking, or chemical treatment) can have a major influence on availability (98, 125). Ruminal adaption is critical in determining the amount of carbohydrate that induces acidosis (86). Telle and Preston (124) showed that, for undernourished sheep, 50 to 60 g of wheat/kg of body weight produced clinical signs of acute acidosis, but well-nourished sheep required 75 to 80 g/kg.

Relatively few studies have evaluated the direct influence of carbohydrate per se on the incidence of laminitis. Manson and Leaver (79) offered a diet of concentrate and silage (60:40 or 40:60 ratio) to cows during wk 3 to 26 of lactation. The TMR of 60:40 concentrate and silage was restricted to yield the same metabolizable energy intake between treatments. Hooves of half of the cows for each treatment were trimmed prior to the experiment; the other half remained untrimmed. The 60:40 diet increased locomotion scores, increased number and duration of clinical lameness, decreased hoof hardness, and increased milk protein; the diet had no effect on milk production compared with the higher forage diet. Trimming hooves reduced the incidence and duration of clinical lamenesses. In addition, hoof growth was significantly increased by trimming. For cows fed the low concentrate diet, 8 cows had an incidence of lameness 3.3 wk in duration; for cows fed the high concentrate diet, 11 cows had an incidence of lameness 3.9 wk in duration.

Because intake was restricted with the 60:40 diet and with grain fed in a TMR, the major difference between dietary treatments was concentrate intake (9.1 vs. 5.8 kg concentrate or 5.7 and 1.7 kg of barley). Cows fed a high amount of concentrate produced 1.2 kg more milk, 0.15 percentage units more protein, and 0.16 kg more milk/kg of DM than did cows fed low amounts of concentrate. This study, therefore, demonstrated the effect of carbohydrate level and availability on lameness, but also showed that increasing nonstructural carbohydrate levels enhanced production performance, at least temporarily.

In another study, Manson and Leaver (77) compared 7 versus 11 kg of concentrate/d from 3 to 22 wk into lactation. Cows fed diets that were high in concentrates had more lameness; sole lesions were the major problem. However, cows fed more grain produced 3.2 kg more milk/d that had 0.06 percentage units higher milk protein. Other researchers (71, 83) have shown a relationship between high carbohydrate diets, feeding frequency, and severity of digital lesions.

The incidence of laminitis can be controlled through good nutrition management (high fiber diets) and use of good feeding and management practices. Increasing concentrate intake to a certain threshold maximizes milk production and milk components.

The manner in which feeds are fed can have a significant impact on the stability of ruminal pH. As the amount of concentrate goes up in the diet or the diet increases in fermentable carbohydrates, saliva production and rumination time decrease, which decreases ruminal pH. Kaufmann et al. (65) showed that feeding frequency of concentrates has a significant impact on maintaining a stable ruminal pH. Nocek (92) found that feeding the same ingredients and forages in different strategies during the day can influence the time ruminal pH remains below a given threshold. The influence of carbohydrate on ruminal pH is the critical link among nutrition, acidosis, and laminitis. Although excessive amounts of ruminally available carbohydrate have been blamed for increased acid production and for overwhelming the bicarbonate buffering systems, a lack of effective fiber can significantly influence ruminal motility, saliva production, and ruminal pH (Figure 10). Ruminal pH is a balance between acid production from carbohydrate substrates and saliva production (buffering action). Substantially more information is needed to quantify physically effective NDF. Digestible NDF can contribute to acid production, especially improperly fermented, wet forages with high nonstructural and carbohydrates and lactic acid levels.

The relationship between ration nonstructural carbohydrate, ruminally available starch, NDF, and eNDF is critical in maintaining proper ruminal function. Poore et al. (105) fed diets that were similar in

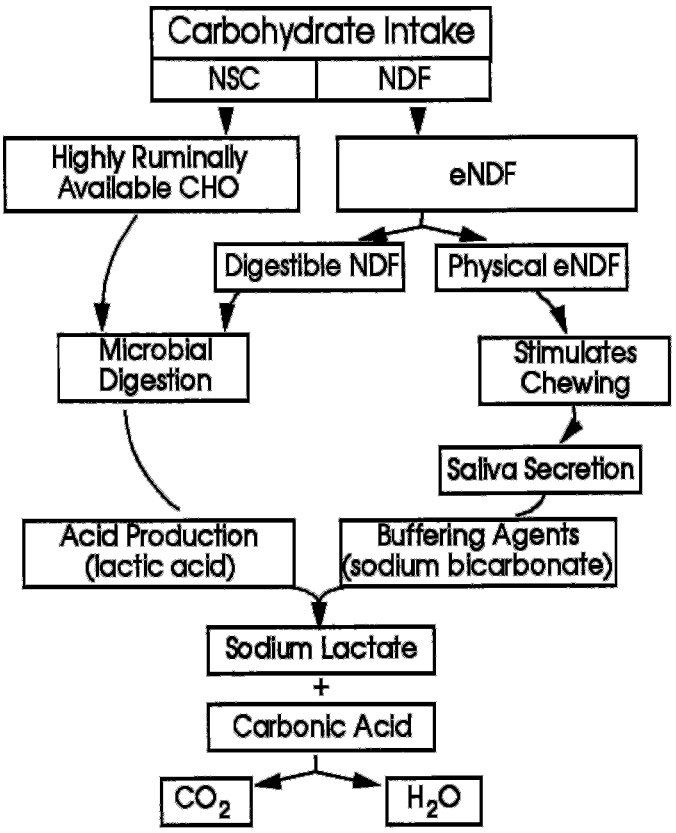

Figure 10. Illustration of structural (NDF) and nonstructural carbohydrate (NSC) on buffering in the rumen. eNDF = Effective NDF.

NDF (30%) in a factorial study in which sorghum was either dry-rolled or steam-flaked and wheat straw was substituted for alfalfa hay. Chopped wheat straw substituted for alfalfa hay did not affect milk yield or composition. Increasing starch degradability increased milk yield and protein, regardless of fiber source. These researchers suggested that a ratio of forage NDF to ruminally degradable starch should be maintained at about 1:1 (wt/wt) to avoid depression in fiber digestion and to maintain normal ruminal function. Nocek and Russell (97) showed milk yield to be maximized when the ratio of nonstructural carbohydrates to NDF was between 0.9 and 1.2.

The addition of hay to diets does less to enhance the effective fiber of the diet than to increase the particle size of silage (10). Although small amounts of hay added to the diet increased intake more than increased silage particle length did, milk production and composition were unaffected by diets that were low in eNDF (10).

Mean values for daily ruminal pH are of questionable validity in evaluating the potential of a given diet to predispose cows to acidosis. More critical to the detriment of certain physiological events is the duration spent under a given pH threshold. Dado and Allen (28) fed diets containing 25 and 35% NDF with and without ruminally inert bulk. Cows fed diets that were low in NDF without ruminally inert bulk had a significantly lower mean ruminal pH. More importantly, the daily minimum pH was lower, and the hours spent at pH <5.5 were higher, for cows that were not fed ruminally inert bulk. Khorasani et al. (66) found that mean ruminal pH was the same (pH 6.06) on diets differing in protein degradability; however, daily minimum pH was significantly different.

Guidelines for Carbohydrate Fractions in Dairy Cows Rations

Based on studies of lactating dairy cows producing >30 kg of milk (88, 99), general guidelines for different carbohydrate fraction concentrations can be considered (percentage of total ration DM): NDF, 25 to 30% (75% from forage); nonstructural carbohydrates, 35 to 40%; and starch, 30 to 40%. When parameters of ruminal degradability are considered, the following are general guidelines: ruminally degradable starch, 60 to 70% of total starch; ruminally degradable NDF, 50 to 60% of total NDF; and ruminally degradable carbohydrate, 50 to 55% of total carbohydrate. These guidelines should only be considered after total ration energy (NE_L) requirements (87) are met for the specific animals in question.

Other guidelines regarding physical form and the ratios of structural to nonstructural carbohydrate include forage NDF to ruminally degradable starch >1:1; NDF:nonstructural carbohydrates >0.9 and <1.2, and eNDF (forage) with 15 to 20% of particles ≥3.8 cm in length.

The method of determination of starch and nonstructural carbohydrate contents and the procedure utilized to determine ruminal degradability can have a significant influence on the analytical measure developed. Particle size, processing method, and moisture content can also significantly influence determinations of ruminal availability. In addition, storage and processing procedures of both structural and nonstructural carbohydrate can dramatically influence ruminal degradability and should be considered in ration formulation. Appropriate N fractions must also be provided with these various carbohydrate fractions for optimal ruminal function and carbohydrate utilization to occur.

Protein in the ration. The amount of protein in the ration has been suggested to influence the incidence of laminitis. Manson and Leaver (78) compared diets with 16.1 versus 19.8% crude protein. The high protein diet significantly influenced locomotion scores and the incidence and duration of clinical lameness for dairy cows between 3 and 26 wk postpartum. Bargari et al. (7) studied the influence of 15.3 versus 18% dietary crude protein on healthy calves and on those affected with laminitis (Table 4). Blood urea N was elevated for both normal and affected calves. Total protein globulin and packed cell volume were elevated in affected calves. Therefore, high percentages of ruminally degradable protein have been identified in association with lameness and laminitis; however, the role of protein is not yet clear.

Little information is available to identify what role protein might play in the development of lameness. Several postulations involve allergic histaminic reactions to certain types of proteins (88) or a link between high protein supplementation and protein degradation end products (9).

TABLE 4. Effect of protein level[1] on laminitis in calves.[2]

Item	Normal farm	Affected farm	
		Normal	Affected
Blood urea, mg/dl	15.9[a]	24.6	25.5
Globulin, g/dl	3.0	2.8[b]	3.9
Total protein, g/dl	6.1	6.1[b]	7.1
Packed cell volume, %	29.4[a]	32.2[b]	33.9
Hemoglobin, %	8.9[a]	9.6	10.1

[a]Different ($P < 0.05$) from affected farm.

[b]Significantly different ($P < 0.05$) from affected animals within affected farm.

[1]Protein level: 15.3% versus 18.0% on normal farms versus farms affected by laminitis.

[2]Bargari et al. (7).

Husbandry Factors Associated with Controlling Subclinical Acidosis and Laminitis

Although carbohydrate nutrition has a direct link to acidosis and laminitis, other factors—including housing, stage of lactation, and age—have an influence on the predisposition of cows to subclinical acidosis and laminitis.

Separation of primiparous heifers into specific groups. Often, laminitis in primiparous heifers is associated with changes in management, such as introduction to groups of mature cows around calving and to stalls with inadequate bedding or poor design such that ease of maneuvering in and out of the stall is difficult. There is a relationship among the time spent standing, the use of stalls, and the incidences of sole ulceration and laminitis in primiparous heifers (52). Colan-Ainsworth et al. (23) showed that supplying additional bedding to stalls eliminated new cases of laminitis and sole ulceration of heifers.

Provision of adequate exercise. Locomotion has a significant influence on the hemodynamics of the peripheral circulation of the foot. Too little exercise (i.e., standing) can cause sluggish blood flow, edema, and swelling. Too much exercise and concussion on concrete floors, especially for heifers that have been accustomed to pasture, can cause trauma and mechanical damage and a greater incidence of sole ulceration (13).

Stall comfort. First, adequate stall space must be provided to allow reclining and ruminating for approximately 12 to 14 h/d. The dimensions of the stall must be proper for the size of animal that is being housed, especially stall length, width, and lunge space. Sand is an optimal stall bedding, providing cow comfort, traction, and lack of organic matter for bacterial growth that may predispose cows to mastitis. However, management of sand may be a challenge because of burrowing and destruction to manure systems. In addition, sand must be free of small stones, which can penetrate the sole horn. An earthen base with shredded tires covered with polyethylene sheets also works effectively in providing a cushioned base. However, this material must not be of an abrasive nature and must not scrape hocks or knees as cows rise and lie down. The use of sawdust with wood chips on these polyethylene surfaces can also be abrasive, causing hock lesions.

Age and stage of lactation. In a survey conducted in the United Kingdom, Rowland et al. (112) showed that susceptibility to lameness increased as age increased; 10-yr-old cows were four times as likely to develop lameness than were 3-yr-old cows. The most prevalent lesions were white line abscesses, sole ulcers, and underrun heels. The incidences of these diseases with age were thought to be caused by cumulative factors (scar tissue).

The same study showed that lameness was more common during the first 120 d postpartum, accounting for 5l% of all cases. Ulcers of the soles were somewhat more common during the 30 d after calving than before calving; white line abscesses, however, were more common toward the end of lactation.

CONCLUSIONS

Bovine lactic acidosis and laminitis are linked through imbalances in carbohydrate nutrition: an excess of ruminally fermentable carbohydrate in con-

junction with inadequate effective fiber. However, laminitis in particular is multifactorial in etiology. In addition, laminitis and acidosis are prevalent during the transition period and are associated with an increased incidence of metabolic and infectious diseases, nutritional mismanagement, and an environment that did not provide cow comfort. The subclinical phases of both disease processes are most costly and damaging because symptoms are often dismissed for other problems. Critical areas of management include practices of feeding and feed management, comfortable cow environment, and routine trimming and care of hooves. More information is needed in order to develop accurate physiological diagnostic indexes that will alert managers to subclinical acidosis and laminitis in the herd (i.e., incidence of sole hemorrhaging, ruminal pH, and milk parameters) before there is a permanent negative influence on production, performance, and health.

REFERENCES

1 Aldrich, J. M., L. D. Muller, G. A. Varga, and L. C. Griel, Jr. 1993. Nonstructural carbohydrate and protein effects on rumen fermentation, nutrient flow, and performance of dairy cows. J. Dairy Sci. 76:1091.

2 Altura, B. M., and B. T. Altura. 1977. Influence of sex hormones, oral contraceptives and pregnancy on vascular muscle and its reactivity. Page 221 *in* Factors Affecting Vascular Reactivity. O. Carrier and S. Shibata, ed. Igaku Shoin, Tokyo, Japan.

3 Andersson, L., and A. Berman. 1980. Pathology of bovine laminitis especially as regards vascular lesions. Acta Vet. Scand. 21:559.

4 Annison, E. F., D. E. Lindsay, and R. R. White. 1963. Metabolic interactions of glucose and lactate in sheep. Biol. Chem. J. 88:3.

5 Atkins, K. B., R. A. Erdman, and J. H. Vandersall. 1988. Dietary choline effects on milk yield and duodenal choline flow in dairy cattle. J. Dairy Sci. 71:109.

6 Bargai, U., and D. Levin. 1992. Lameness in the Israeli dairy herd, prevalence, types, distribution and estimated cost. Isr. J. Vet. Med. 48:88.

7 Bargai, U., I. Schamia, A. Lublin, and E. Bogin. 1992. Winter outbreaks of laminitis in dairy calves: etiology and laboratory, radiological and pathological findings. Vet. Rec. 131:411.

8 Barry, M. C., D. G. Fox, T. P. Tylutki, A. N. Pell, J. D. O'Connor, C. J. Sniffen, and W. Chalupa. 1994. A Manual for Using the Cornell Net Carbohydrate and Protein System for Evaluating Cattle Diets. Release No. 3. Cornell Univ., Ithaca, NY.

9 Bazeley, K., and P.J.N. Pinsent. 1984. Preliminary observations on a series of outbreaks of acute laminitis in dairy cattle. Vet. Rec. 115:619.

10 Beauchemin, J. A., B. I. Farr, L. M. Rode, and G. B. Schaalje. 1994. Effects of alfalfa silage chopped length and the supplementary long hay on chewing and milk production of dairy cows. J. Dairy Sci. 77:1526.

11 Bergsten, C. 1992. Subclinical laminitis: studies on risk factors in first calf heifers. Page 55 *in* Proc. 7th Int. Symp. Disorders Ruminant Digit, June 21–25, Rebild, Denmark.

12 Bergsten, C. 1993. A photometric method for recording hoof diseases in cattle, with special reference to hemorrhages of the sole. Acta Vet. Scand. 34:281.

13 Bergsten, C. 1994. Hemorrhages of the sole horn of dairy cows as a retrospective indicator of laminitis: an epidemiological study. Acta Vet. Scand. 35:55.

14 Boosman, R., J. Koeman, and R. Knap. 1989. Histopathology of the bovine pododerma in relation to age and chronic laminitis. J. Vet. Med. 36:438.

15 Boosman, R., F. Nemeth, E. Gruys, and A. Klarenbeck. 1989. Arteriographical and pathological changes in chronic laminitis in dairy cattle. Vet. Q. 11:144.

16 Bradley, H. K., D. Shannan, and D. R. Neilson. 1989. Subclinical laminitis in dairy heifers. Vet. Rec. 125:177.

17 Brent, B. E. 1976. Relationship of acidosis to other feedlot ailments. J. Anim. Sci. 43:930.

18 Brownlee, A. 1956. The development of ruminal papillae in cattle fed different diets. Br. Vet. J. 112:369.

19 Bruce, L. A., and T. L. Huber. 1973. Inhibitory effects of acid in the intestine on rumen motility in sheep. J. Anim. Sci. 37: 164.

20 Cameron, M. R., T. H. Klusmeyer, G. L. Lynch, J. H. Clark, and D. R. Nelson. 1991. Effects of urea and starch on rumen fermentation, nutrient passage to the duodenum, and performance of cows. J. Dairy Sci. 74:1321.

21 Casper, D. P., and D. J. Schingoethe. 1986. Evaluation of urea and dried whey in diets of cows during early lactation. J. Dairy Sci. 69:1346.

22 Chavance, J. 1946. Histamine theory and treatment of laminitis Vet. Med. 41:199.

23 Colan-Ainsworth, P., G. A. Lunn, R. C. Thomas, and R. G. Eddy. 1989. Behavior of cows in cubicles and its possible relationship with laminitis in replacement heifers. Vet. Rec. 125:573.

24 Coppock, C. E., G. T. Schelling, F. M. Byers, J. W. West, J. M. Labore, and C. E. Gates. 1986. A naturally occurring mineral as a buffer in the diet of lactating dairy cows. J. Dairy Sci. 69: 111.

25 Counotte, G. H., R. A. Prins, R.A.M. Janssen, and M.J.A. de Bie. 1981. Role of *Megasphera elsdenii* in the fermentation of DL-[2-^{13}C]lactate in the rumen of dairy cattle. Appl. Environ. Microbiol. 42:649.

26 Cricklow, E. C., and R. K. Chaplin. 1985. Ruminal lactic acidosis: relationship of forestomach motility to nondissociated volatile fatty acid levels. Am. J. Vet. Res. 46:1908.

27 Cummins, K. A., J. E. Nocek, and C. E. Polan. 1982. Growth and nitrogen of calves fed rations of varying nitrogen degradability and physical form. J. Dairy Sci. 65:773.

28 Dado, R. G., and M. S. Allen. 1995. Intake limitations, feeding behavior, and rumen of cows challenged with rumen fill from dietary fiber or inert bulk. J. Dairy Sci. 78:118.

29 Dain, J. L., A. L. Neal, and R. W. Dougherty. 1955. The occurrence of histamine and tyramine in rumen ingesta of experimentally overfed sheep. J. Anim. Sci. 14:930.

30 DePeters, E. J., and S. J. Taylor. 1985. Effects of feeding corn or barley on composition of milk and diet digestibility. J. Dairy Sci. 68:2027.

31 DeVisser, H., P. L. VanDerTogt, and S. Tamminga. 1990. Structural and non-structural carbohydrates in concentrate supplements of silage-based dairy cow rations. 1. Feed intake and milk production. Neth. J. Agric. Sci. 38:487.

32 Dewes, H. F. 1978. Some aspects of lameness in dairy herds. N.Z. Vet. J. 26:147.

33 Dirksen, G. 1989. Rumen function and disorders related to production disease. Page 350 *in* Proc. VII Int. Conf. Dis. Farm Anim. Cornell Univ., Ithaca, NY.

34 Dirksen, V. G., H. G. Liebich, G. Brosi, H. Hagemeister, and E. Mayer. 1984. Rumen mucosa morphology and fatty acid absorption-significant factors for health and production. Zentralbl. Veterinaermed. 31:414.

35 Dougherty, R. W., K. W. Corburn, H. M. Cock, and M. J. Allison. 1975. Preliminary study of the appearance of endotoxins in circulatory system of sheep and cattle after induced grain engorgement. Anim. J. Vet. Res. 36:831.

36 Dunlap, R. H., and P. B. Hammond. 1965. D-lactic acidosis of ruminant. Ann. New York Acad. Sci. 119:1109.
37 Eddy, R. G., and C. P. Scott. 1980. Some observations on the incidence of lameness in dairy cattle in Somerset. Vet. Rec. 106:140.
38 Edwards, G. B. 1982. Acute and sub-acute laminitis in cattle. Vet. Annu. 22:99.
39 Enevoldsen, C., Y. T. Grohn, and I. Thysen. 1991. Sole ulcers in dairy cattle: association with season, cow characteristics, disease, and production. J. Dairy Sci. 74:1284.
40 Feng, P., W. H. Hoover, T. K. Miller, and R. Blauwiekel. 1993. Interactions of fiber and nonstructural carbohydrates on lactation and ruminal function. J. Dairy Sci. 76:1324.
41 Fischer, J. M., J. G. Buchanan-Smith, C. Campbell, G. G. Grieve, and O. B. Allen. Effects of forage particle size and long hay for cows fed total mixed rations based on alfalfa and corn. J. Dairy Sci. 77:217.
42 Fulton, W., T. J. Klopfenstein, and R. A. Britton. 1979. Adaptation to high concentrate diets by beef cattle. I. Adaptation to corn and wheat diets. J. Anim. Sci. 49:775.
43 Fulton, W. R., T. J. Klopfenestein, and R. A. Britton. 1979. Adaptation to high concentrate diets by beef cattle. II. Effect of ruminal pH alteration on rumen fermentation and voluntary intake of wheat diets. J. Anim. Sci. 49:785.
44 Garrett, E. F., M. N. Pereira, L. E. Armentano, K. V. Nordlund, and G. R. Oetzel. 1995. Comparison of pH and VFA concentration of ruminal fluid from dairy cows collected through a rumen cannula vs. ruminocentesis. J. Dairy Sci. 78: (Suppl. 1):299.(Abstr.)
45 Gentile, G., S. Cinotti, G. Ferri, and P. Famigli-Bergamini. 1986. Nutritional acidosis and technological characteristics of milk in high producing dairy cows. Page 823 *in* Proc. 14th World Congr. Diseases Cattle. P. J. Harigan and M. L. Monaghan, ed. Dublin, Ireland.
46 Ghorbani, G. R., J. A. Jackson, and R. W. Hemken. 1989. Effects of sodium bicarbonate and sodium sesquicarbonate on animal performance, ruminal metabolism, and systemic acid-base status. J. Dairy Sci. 72:2039.
47 Giesecke, D., and M. Stangassinger. 1980. Lactic acid metabolism. Page 523 *in* Physiology and Metabolism in Ruminants. AVI Publ. Co., Inc., Westport, CT.
48 Goth, A. 1974. Medical Pharmacology. 7th ed. C. B. Mosby Co., St. Louis, MO.
49 Grant, R. J., V. F. Colenbrander, and D. R. Mertens. 1990. Milk fat depression in dairy cows: role of particle size of alfalfa hay. J. Dairy Sci. 73:1823.
50 Grant, R. J., V. F. Colenbrander, and D. R. Mertens. 1990. Milk fat depression in dairy cows: role of silage particle size. J. Dairy Sci. 73:1834.
51 Greenough, P. R. 1982. Laminitis review. Page 1 *in* Proc. 4th Int. Symp. Disorders Ruminant Digit. October 7–10. Ecole Natl. Vet. d'Alfort, Paris, France.
52 Greenough, P. R., F. J. MacCallum, and A. D. Weaver. 1972. Lameness in Cattle. J. B. Lippincott, Philadelphia, PA.
53 Greenough, P. R., and J. J. Vermunt. 1991. Evaluation of subclinical laminitis in a dairy herd and observations on associated nutritional and management factors. Vet. Rec. 128:11.
54 Grohn, Y. T., and M. L. Bruss. 1990. Effective diseases, production, and season on traumatic reticuloperitonitis and ruminal acidosis in dairy cattle. J. Dairy Sci. 73:2355.
55 Harmon, D. L., R. A. Britton, and R. L. Prior. 1983. Influence of diet on glucose turnover and rates of gluconeogenesis, oxidation and turnover of D-(–)-lactate in the bovine. J. Nutr. 113: 1842.
56 Harmon, D. L., R. A. Britton, R. L. Prior, and R. A. Stock. 1985. Net portal absorption of lactate in volatile fatty acids in steers experiencing glucose induced acidosis or fatty 70% concentrate diet ad libitum. J. Anim. Sci. 60:560.
57 Hession, A. O., and L. Kung. 1992. Altering ruminal fermentation by microbial inoculation with lactate utilizing microorganism. J. Anim. Sci. 70(Suppl. 1):311.(Abstr.)
58 Huber, T. L. 1971. Effect of acute indigestion of compartmental water volumes and osmolarity in sheep. Am. J. Vet. Res. 32:887.
59 Huber, T. L. 1976. Physiological effects of acidosis on feed lot cattle. J. Anim. Sci. 43:902.
60 Huhtanen, P., H. Miettinen, and M. Ylinen. 1993. Effect of increasing ruminal butyrate on milk yield and blood constituents in dairy cows fed a grass silage-based diet. J. Dairy Sci. 76:1114.
61 Huntington, G. B. 1988. Acidosis. Page 474 *in* The Ruminant Animal: Digestive Physiology and Nutrition. D. C. Church, ed. Prentice-Hall, Englewood Cliffs, NJ.
62 Huntington, G. B., and R. A. Britton. 1979. Effective dietary lactic acid on rumen lactate metabolism and blood acid base stasis of lambs switched from low to high concentrate diets. J. Anim. Sci. 49:1569.
63 Johnson, M. A., T. F. Sweeney, and L. D. Muller. 1988. Effects of feeding synthetic zeolite A sodium bicarbonate on milk production nutrient digestion, and rate of digesta passage in dairy cows. J. Dairy Sci. 71:946.
64 Jubb, K. V., and P. C. Kennedy. 1970. Pathology of Domestic Animals. 2nd ed. Vol. 2. Academic Press, New York, NY.
65 Kaufmann, W., H. Hagemeister, and G. Dirksen. 1980. Adaptation to changes in dietary composition, level and frequency of feeding. Page 587 *in* Physiology and Metabolism of Ruminants. AVI Publ. Co., Westport, CT.
66 Khorasani, G. R., G. DeBoer, B. Robinson, and J. J. Kennelly. 1994. Influence of dietary protein in starch on production and metabolic responses in dairy cows. J. Dairy Sci. 77:813.
67 Klusmeyer, T. H., G. L. Lynch, and J. H. Clark. 1991. Effects of calcium salts of fatty acids and protein source on ruminal fermentation and nutrient flow to duodenum of cows. J. Dairy Sci. 74:2206.
68 Kostyra, E., J. Jaworski, T. Glazer, M. Rusiecki, T. Janowski, and A. Ras. 1993. Changes in composition of nitrogen compounds of milk caused by acute experimental acidosis in the cow. Acta Acad. Agric. Tecn. Olstenensis Vet. 11:118.
69 Kung, L., and A. O. Hession. 1995. Preventing in vitro lactate accumulation in ruminal fermentations by inoculation of *Megasphera elsdenii*. J. Anim. Sci. 73:250.
70 Liebich, H. G., G. Dirksen, A. Arbel, S. Dori, and E. Mayer. 1987. Feed dependent changes in the ruminal mucosa on high producing cows during the dry period and first eight weeks postpartum. J. Vet. Med. 34:661.
71 Livesey, C. T., and F. L. Fleming. 1984. Nutritional influences on laminitis, sole ulcer and bruised sole in Friesian cows. Vet. Rec. 114:510.
72 Mackie, R. I., F.M.C. Gilcrest, and S. Heath. 1984. In vivo study of ruminal microorganisms influencing lactate turnover and its contribution to volatile fatty production. J. Agric. Sci. 103:37.
73 Maclean, C. W. 1965. Observations on acute laminitis of cattle in South Hampshire. Vet. Rec. 77:662.
74 Maclean, C. W. 1966. Observations on laminitis and intense beef units. Vet. Rec. 78:223.
75 Maclean, C. W. 1970. The hematology of bovine laminitis. Vet. Rec. 86:710.
76 Maclean, C. W. 1971. The histopathology of laminitis in dairy cows. J. Comp. Pathol. 81:25.
77 Manson, F. J., and J. D. Leaver. 1988. The influence of concentrate amount on locomotion and clinical lameness in dairy cattle. Anim. Prod. 47:185.
78 Manson, F. J., and J. D. Leaver. 1988. The influence of dietary protein intake and of hoof trimming on lameness in dairy cattle. Anim. Prod. 47:191.
79 Manson, F. J., and J. D. Leaver. 1989. The effect of concentrates: silage ratio and hoof trimming on lameness in dairy cattle. Anim. Prod. 49:15.
80 McCarthy, R. D., Jr., T. H. Klusmeyer, J. L. Vicini, and J. H. Clark. 1989. Effects of source of protein and carbohydrate on ruminal fermentation and passage of nutrients to the small intestine of lactating cows. J. Dairy Sci. 72:2002.

81 Merck and Co. 1976. Merck Index. Page 619 *in* Encyclopedia of Chemicals and Drugs. 9th ed. M. Windholz, ed. Merck and Company, Inc., Rahway, NJ.
82 Mgassa, M. N., G. Amaya-Posada, and M. Hesselholt. 1984. Pododermitis aseptica diffusa (laminitis) in free range beef cattle in tropical Africa. Vet. Rec. 115:413.
83 Mortensen, K. 1994. Bovine laminitis (diffuse aseptic pododermitis): clinical and pathological findings. Page 210 *in* Proc. 8th Int. Symp. Disorders Ruminant Digits Int. Conf. Bovine Lameness. P. Greenough, ed. Saskatoon, Saskatchewan and Banff, Alberta, Canada.
84 Mullenax, C. H., R. F. Keeler, and M. J. Allison. 1966. Physiological response of ruminants to toxic factors extracted from rumen bacteria and rumen fluid. Anim. J. Vet. Res. 27:857.
85 Nagaraja, T. G., and G. Town. 1990. Ciliated protozoa in relation to ruminal acidosis and lactic acid metabolism. Page 194 *in* Rumen Ecosystem: Microbial Metabolism and Regulation. R. Oneora, H. Minato, and H. Itabashi, ed. Springer-Verlag, New York, NY.
86 Nagel, S., and G. A. Broderick. 1992. Effect of formic acid or formaldehyde treatment of alfalfa silage on nutrient utilization by dairy cows. J. Dairy Sci. 75:140.
87 National Research Council. 1989. Nutrient Requirements of Dairy Cattle. 6th rev. ed. Natl. Acad. Sci., Washington, DC.
88 Nilsson, S. A. 1963. Clinical morphological and experimental studies of laminitis in cattle. Acta Vet. Scand. 4(Suppl. 1):1.
89 Nisbet, D. J., and S. Martin. 1994. Factors affecting L-lactate utilization by *Selenomonas ruminantium*. J. Anim. Sci. 72: 1355.
90 Nocek, J. E. 1986. Bovine foot anatomy: a functional and practical perspective. Prof. Anim. Sci. 2:1.
91 Nocek, J. E. 1987. Characterization of in situ dry matter and nitrogen in various corn grain forms. J. Dairy Sci. 70:2291.
92 Nocek, J. E. 1992. Feeding sequence and strategy effects on ruminal environment and production performance in first lactation cows. J. Dairy Sci. 75:3100.
93 Nocek, J. E., C. W. Heald, and C. E. Polan. 1984. Influence of ration of physical form and nitrogen availability on ruminal morphology of growing bull calves. J. Dairy Sci. 67:334.
94 Nocek, J. E., J. H. Herbein, and C. E. Polan. 1980. Influence of ration physical form rumen degradable nitrogen and age on rumen epithelial propionate and acetate transport and some enzymatic activities. J. Nutr. 110:2355.
95 Nocek, J. E., and E. M. Kessler. 1980. Growth and rumen characteristics of Holstein steers fed pelleted or conventional diets. J. Dairy Sci. 63:249.
96 Nocek, J. E., and C. E. Polan. 1984. Influence of ration physical form of nitrogen availability on rumen fermentation patterns and plasma of growing bull calves. J. Dairy Sci. 67:1038.
97 Nocek, J. E., and J. B. Russell. 1988. Protein and energy as an integrated system. Relationship of ruminal protein and carbohydrates availability to microbial synthesis and milk production. J. Dairy Sci. 71:2070.
98 Nocek, J. E., and S. Tamminga. 1991. Site of digestion of starch in the gastrointestinal tract of dairy cows and its effect on milk yield and composition. J. Dairy Sci. 74:3598.
99 Norlund, K. V. 1995. Herd based rumenocentesis: a clinical approach to the diagnosis subacute rumen acidosis. Page 1 *in* Northeast Med. Symp. R. Saltman, ed. Syracuse, NY.
100 Nordlund, K. V., and E. F. Garrett. 1994. Rumenocentesis: a technique for collecting rumen fluid for the diagnosis of subacute rumen acidosis in dairy herds. Bovine Pract. 28:109.
101 Olivera, J. S., J. T. Huber, D. Ben-Ghedalia, R. S. Swingle, C. B. Theurer, and M. Pessarkli. 1993. Influence of sorghum grain processing on performance of lactating dairy cows. J. Dairy Sci. 76:575.
102 Ossent, P., and C. J. Lischer. 1994. Theories on the pathogenesis of bovine laminitis. Page 207 *in* Proc. 8th Int. Symp. Disorder Rumin. Digit Int. Conf. Bovine Lameness. P. R. Greenough, ed. Saskatoon, Saskatchewan and Banff, Alberta, Canada.
103 Petit, H. V., and D. M. Veira. 1991. Effect of grain level and protein source on ruminal fermentation, degradability, and digestion in milking cows fed silage. J. Dairy Sci. 74:2256.
104 Philipot, J. M., P. Pluvinage, and F. Luquet. 1994. Clinical characterization of a syndrome by ecopathology methods: an example of dairy cow lameness. Vet. Res. 25:239.
105 Poore, M. H., J. A. Moore, R. S. Swingle, T. E. Eck, and W. H. Brown. 1993. Response of lactating Holstein cows to diets varying in fiber source and rumen starch degradability. J. Dairy Sci. 76:2235.
106 Prentice, D. E., and P. A. Neal. 1972. Some observations on the incidence of lameness in dairy cattle in West Cheshire. Vet. Rec. 91:1.
107 Reilly, P.E.B., and L. G. Chandrasena. 1977. Sheep lactate entry measurements: error to sampling jugular blood. Am. J. Physiol. 233:E138.
108 Reilly, P.E.B., and L. G. Chandrasena. 1978. Glucose lactate interactions in sheep. Am. J. Physiol. 235:E487.
109 Robinson, J. A., W. J. Smolenski, R. C. Greening, M. L. Ogilvie, R. L. Bell, K. Barsuhn, and J. P. Peters. 1992. Prevention of acute acidosis and enhancement of feed intake in the bovine by *Megasphera elsdenii* 407A. J. Anim. Sci. 70(Suppl. 1):310. (Abstr.)
110 Robinson, P. H., and R. E. McQueen. 1992. Influence of rumen fermentable neutral detergent fiber levels on feed intake and milk production of dairy cows. J. Dairy Sci. 75:520.
111 Rodwell, A. W. 1953. The occurrence and distribution of amino acid decarboxylases within the genus lactobacillus. J. Gen. Microbiol. 8:222.
112 Rowland, G. J., A. M. Russell, and L. A. Williams. 1985. Effects of stage of lactation, month, age, origin and heart girth on lameness in dairy cattle. Vet. Rec. 117:576.
113 Russell, A. M., J. G. Rollands, R. S. Shaw, and A. D. Weaver. 1982. Survey of lameness in British cattle. Vet. Rec. 111:155.
114 Russell, J. B. 1986. Ecology of rumen microorganisms: energy use. Page 74 *in* Aspects of Digestive Physiology and Ruminates. Proc. 30th Int. Congr. Int. Union Physiological Sci. Proc. A. Dobson and M. Dobson, ed. Cornell Univ. Press, Ithaca, NY.
115 Russell, J. B., and T. Hino. 1985. Regulation of lactate production in streptococcus bovis: a spiraling effect that contributes to rumen acidosis. J. Dairy Sci. 68:1712.
116 Russell, J. B., W. M. Sharp, and R. L. Baldwin. 1979. The effect of pH on maximum bacterial growth rate and its possible role as a determinant of bacterial competition in the rumen. J. Anim. Sci. 48:251.
117 Sanford, J. 1963. Formation of histamine in ruminal fluid. Nature (Lond.) 199:829.
118 Sarwar, M., J. L. Firkins, and M. L. Eastridge. 1992. Effects of varying forage and concentrate carbohydrates on nutrient digestibilities and milk production by dairy cows. J. Dairy Sci. 75:1533.
119 Stangassinger, M., and D. Giesecke. 1978. Untersuchunger zur Genese und. Biochemie o'er Pansenacidose 6. Renal Ausscheidung von Michsaure-Isomeren. Zentralb. Veterinaermed. Reihe A 25:597.
120 Stock, R., and R. A. Britton. 1993. Acidosis in feedlot cattle. Page A1 *in* Scientific Update on Rumensin/Tylan for the Professional Feedlot Consultant. Elanco Anim. Health, Indianapolis, IN.
121 Stokes, M. R., L. L. Vandemark, and L. S. Bull. 1986. Effects of sodium bicarbonate, magnesium oxide, and a commercial buffer mixture in early lactation cows fed haycrop silage. J. Dairy Sci. 69:1595.
122 Stokes, S. R., W. H. Hoover, T. K. Miller, and R. Blauweikel. 1991. Ruminal digestion and microbial utilization of diets varying in type of carbohydrate and protein. J. Dairy Sci. 74: 871.
123 Strobel, H. J., and J. B. Russell. 1986. Effect of pH and energy spilling on bacterial protein synthesis by carbohydrate-limited cultures of mixed rumen bacteria. J. Dairy Sci. 69:2941.

124 Telle, P. P., and R. L. Preston. 1971. Bovine lactic acidosis: intra-ruminal and systemic. J. Anim. Sci. 33:698.
125 Theurer, C. D. 1986. Grain processing effects on starch utilization by ruminants. J. Anim. Sci. 63:1649.
126 Toussant-Raven, E. 1982. Some reflections after three symposia on bovine digital disorders. Page *in* Proc. 4th Int. Symp. Int. Disorders Rumin. Digit. October 7–10. Ecole Natl. Vet. D'Alfort, Paris, France.
127 Tranter, W. P., and R. S. Morris. 1991. A case study of lameness in three dairy herds. N.Z. Vet. J. 39:88.
128 Tranter, W. P., R. S. Morris, and N. B. Williamson. 1991. A longitudinal study of the hooves on non-lame cows. N.Z. Vet. J. 39:53.
129 Tucker, W. B., G. A. Harrison, and R. W. Hemken. 1988. Influence of dietary cation-anion balance on milk, blood, urine, and rumen fluid in lactating dairy cattle. J. Dairy Sci. 71:346.
130 Valdez, F. R., J. H. Harrison, and S. C. Fransen. 1989. Effect of feeding silage of early and late maturing corn planted at two population densities to lactating dairy cows. J. Dairy Sci. 72: 2081.
131 Vermunt, J. J. 1994. Predisposing causes of laminitis. Page 236 *in* Proc. 8th Int. Symp. Disorders Ruminant Digits Int. Conf. Bovine Lameness. G. R. Greenough, ed. Saskatoon, Saskatchewan, Canada. Banff, Alberta, Canada.
132 Voelker, H. H., D. P. Casper, F. C. Ludens, and D. J. Schingoethe. 1989. High moisture corn preserved with esters of propionic acid for lactating cows. J. Dairy Sci. 72:89.
133 Wagner, K. M., J. L. Firkins, M. L. Eastridge, and B. L. Hull. 1993. Replacement of corn silage with wheat middlings and calcium chloride or sodium bicarbonate for lactating dairy cows. J. Dairy Sci. 76:564.
134 Weekes, T.E.C. 1972. Effects of pregnancy in lactation in sheep on the metabolism of propionate by the ruminal mucosa and on some enzymatic activities in the ruminal mucosa. J. Agric. Sci. (Camb.) 79:409.
135 Weigand, E. J., W. Young, and A. D. McGilliard. 1975. Volatile fatty acid metabolism of rumen mucosa fed from cattle fed hay or grain. J. Dairy Sci. 58:1294.
136 Wells, S. J., A. M. Trent, W. E. Marsh, P. G. McGovern, and R. A. Robinson. 1993. Individual cow risk factors for clinical lameness in lactating dairy cows. Prev. Vet. Med. 17:95.
137 Whitaker, D. A., J. M. Kelly, and E. J. Smith. 1983. Incidence of lameness in dairy cows. Vet. Rec. 113:60.
138 Whitehurst, G. B., D. C. Beitz, M. A. Pothoven, R. Ellison, and M. H. Crump. 1978. Lactate as a precursor of fatty acids in bovine adipose tissue. J. Nutr. 108:1806.