Relationship of vitamin E supplementation and antimicrobial treatment with acute-phase protein responses in cattle affected by naturally acquired respiratory tract disease

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Objective—To correlate serum concentrations of fibrinogen (Fib), haptoglobin (Hap), serum amyloid-A (SAA), and α-1 acid glycoprotein (AGP) with clinical respiratory tract disease and response to treatment in transport-stressed feedlot cattle fed vitamin E-supplemented diets.

Animals—387 heifer calves (mean initial weight, 197 kg).

Procedure—Calves purchased from an order buyer were delivered to a feedlot to study the effects of dietary supplementation with 2,000 IU of vitamin E for 0, 7, 14, or 28 days after arrival. Serum or plasma Fib, Hap, SAA, and AGP concentrations were measured on days 0, 7, and 28 after arrival as well as at the time of treatment for respiratory tract disease with antimicrobial drugs and after completion of treatment.

Results—Vitamin E supplementation was associated with decreased treatment costs. In cattle that were not recognized as sick or responded positively to 1 antimicrobial treatment, serum Hap concentrations were significantly lower on days 0 and 7 than concentrations for cattle that required > 1 treatment. Serum Hap concentrations and ratios of Hap to SAA on day 0 significantly correlated with the number of antimicrobial treatments required. Serum Hap concentrations at the time of initial treatment were significantly lower for cattle that required only 1 treatment, compared with those that required > 1 treatment.

Conclusions and Clinical Relevance—Serum Hap concentrations are of potential value for use in assessing feedlot cattle that may become ill as a result of respiratory tract disease and for use in monitoring treatment efficacy. (*Am J Vet Res* 2002; 63:1111–1117)

Bovine respiratory disease complex (BRDC) continues to affect the economic viability of the beef cattle industry despite the use of numerous vaccines and antimicrobial drugs to control the problem.[1-5] In 1995, BRDC cost beef cattle producers nearly $500 million.[6] The most common infectious agents associated with BRDC are *Mannheimia haemolytica*, *Pasteurella multocida*, *Haemophilus somnus*, **bovine herpesvirus type 1 (BHV-1)**, **bovine viral diarrhea virus (BVDV)**, **parainfluenza virus type 3 (PI3)**, and **bovine respiratory syncytial virus (BRSV)**.[4] Substantial epidemiologic and experimentally derived data have been used to document the relationship between viral and bacterial pathogens and their combined contribution to the incidence of pneumonia in cattle.[4,7-9] The complexity of this pathogenic synergism makes accurate diagnosis and treatment difficult. Development of an analytic tool to indicate the health status of feedlot cattle would be valuable to food animal veterinarians as well as the beef cattle industry.[10] Measurement of concentrations of serum or plasma acute-phase proteins in cattle has potential as diagnostic and prognostic tools.[5] Acute-phase proteins are rapidly synthesized and secreted by the liver in response to certain cytokines, bacterial or viral infections, toxic insults, or other stressors. Their function is to minimize cellular damage and to promote the repair of damaged tissue.[11-14]

In human and veterinary medicine, several acute-phase proteins commonly are measured, including **fibrinogen (Fib)**, **haptoglobin (Hap)**, **serum amyloid-A (SAA)**, **α-1-acid glycoprotein (AGP)**, ceruloplasmin, α-2-macroglobulin, and C-reactive protein.[10,13,14-16] Certain cytokines (interleukin-1, interleukin-6, and tumor-necrosis factor-α), which modulate immune function and can stimulate the acute-phase response, are themselves often considered acute-phase proteins.[17,18] Measurement of acute-phase proteins during various disease states is of interest for use as prognostic indicators and in monitoring therapeutic efficacy.

Concentrations of many acute-phase proteins are negligible in healthy cattle, but these acute-phase proteins are easily detectable during an acute infection.[19] Serum Fib concentration is recognized as the most commonly used assay of acute-phase proteins in cattle.[19] However, Hirvonen et al[10] suggested that use of Fib concentrations has distinct limitations as a prognostic tool. Serum concentrations of acute-phase proteins are clearly increased in response to clinical infection or stress in cattle.[13,20,21] In other studies,[3,5,22] it has been suggested that measurement of Hap concentrations could be a highly effective prognostic tool for monitoring antimicrobial drug efficacy. Concentrations

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of SAA can be clinically useful for monitoring sick cattle, especially when the **ratio of Hap to SAA (Hp:SAA)** is examined.[21,23]

The objective of the study reported here was to compare serum concentrations of 4 acute-phase proteins (Fib, Hap, SAA, and AGP) and determine their use as prognostic or diagnostic tools regarding BRDC in marketing- and transport-stressed feedlot cattle fed diets supplemented with vitamin E for varying lengths of time. These cattle were part of a study in which the effects of vitamin E supplementation of rations fed to cattle newly arrived at a feedlot were examined.

Materials and Methods

Animals—A total of 387 heifer calves (mean initial weight, 197 kg) were delivered in 4 separate shipments to a beef research facility near the campus of Oklahoma State University. These cattle were on a 42-day feeding trial to determine whether daily feeding of 2,000 IU of vitamin E in diets of newly arrived cattle for 0, 7, 14, or 28 days would have an effect on performance and treatment costs.

Experimental design—Briefly, cattle were purchased through an order buyer and transported to the feedlot in truckload consignments between early August 1999 and late December 1999. Mean daily temperature ranged from 32 to 40.6 C in August and from 4.5 to 24 C in December. On the day of arrival at the feedlot, calves were allowed to commingle and rest for at least 1 hour in a processing facility prior to initial procedures that included assessment of overall health, determination of weight of each calf, and insertion of a sequentially numbered identification tag in the left ear of each calf. Calves were randomly allocated among 6 holding pens and fed prairie hay and a complete ration. Calves remained in the holding pens for up to 36 hours before entrance into the study.

On the day of initial processing (day 0), calves were weighed, vaccinated against 4 major BRDC viruses (BHV-1, PI3, BVDV, and BRSV; 2 ml injected IM),[a] vaccinated against *Clostridium* spp (2 ml injected SC),[b] and injected with a product[c] for control of internal and external parasites (1 ml/50 kg, SC). Viral vaccines were administered again on day 14. Calves were blocked on the basis of weight of each calf into 2 weight classifications (ie, light and heavy) and randomly assigned to 1 of 4 dietary groups. Cattle in each group were fed 2,000 IU of vitamin E for 0 (control group), 7, 14, or 28 days (groups E7, E14, or E28, respectively). Vitamin E-supplemented diets were randomly assigned to be fed to 8 pens of cattle (4 pens of light cattle and 4 pens of heavy cattle). Pen size (12.2 × 30.5 m) was uniform for all pens, and adjacent pens shared automatic water basins. Feed was delivered once daily at approximately 7 AM, except during inclement weather when it was delivered twice daily to provide clean, dry feed for a majority of each day. Cattle were weighed on days 0, 14, 28, and 42. Serum and plasma samples were obtained from 12 cattle/group on days 0, 7, and 28 and used for determination of concentrations of acute-phase proteins.

Cattle were closely observed each morning at approximately 6:30 AM for signs of respiratory tract disease as well as other diseases. Signs monitored included lethargy, inappetence, cough, weakness, and ocular or nasal discharge. Calves that had 2 or more of those signs and that had a rectal temperature of > 40 C were administered antimicrobial treatment. Initial antimicrobial treatment consisted of administration of tilmicosin[d] (10 mg/kg, SC). If a calf failed to respond to tilmicosin, it was treated with florfenicol[e] (40 mg/kg, SC). If the calf also failed to respond to administration of florfenicol, ceftiofur hydrochloride[f] was administered (2.2 mg/kg, SC). Additionally, whenever a calf was designated as sick, 1 plasma and 1 serum sample were obtained for determination of concentrations of acute-phase proteins. Two weeks after initial antimicrobial treatment for respiratory tract disease, health status of the treated calf was assessed. If additional clinical signs were not evident, another set of plasma and serum samples was obtained at that time for analysis of acute-phase protein concentrations.

Measurement of acute-phase proteins—Plasma Fib concentration was determined by use of heat precipitation (60 C for 3 minutes) and refractometry of a vortexed sample, as described elsewhere.[24] Serum Hap concentration was determined by use of commercial radial immunodiffusion kits for bovine Hap.[g] The coefficient of variation stated by the manufacturer was < 4% for repeated, identical measurements of the same test sample. Concentration of SAA was determined by use of a commercial ELISA kit[h] used in accordance with the manufacturer's recommendations. The SAA concentration was determined by measuring the optical density at a wavelength of 490 nm by use of an automated plate reader.[i] Bovine AGP radial immunodiffusion kits[j] were used to determine the serum concentration of AGP in samples; the kits were used in accordance with the manufacturer's recommendations.

Serologic examination—Concentrations of serum antibodies against 4 major BRDC viruses were determined on day 0 for all calves and on days 14, 28, and 42 for 7 calves/group. The same calves were used for sample collection on each day. Concentrations of serum antibodies against BHV-1, BVDV, PI3, and BRSV were measured by use of virus-neutralization assays by personnel at a diagnostic laboratory.[k]

Statistical analysis—All data were analyzed by use of a statistical program.[l] Analysis of variance procedures were used to assess the effects of time, dietary vitamin E group, and number of antimicrobial treatments each sick calf was administered on the responses of interest. Least-squares means were examined for differences among the factors of interest. Multiple comparisons (least significant difference procedure) were used to determine significant changes in acute-phase protein concentrations and viral-neutralization titers. Correlations were assessed to determine the relationship between the responses and the number of treatments the calves received.

Results

Clinical disease—We detected variation among the 4 truckloads of calves in regard to morbidity (37.7 to 74.1%) attributable to respiratory tract disease (**Table 1**). Overall, 225 of 387 (58.1%) calves had clinical signs of respiratory tract disease and were treated. Two calves (0.5%) in the first truckload died between 7 and 14 days after arrival; necropsy revealed lesions of fibrinous pleuropneumonia typical of bovine pneumonic pasteurellosis. Those 2 calves died during a period of severe heat in August. However, there were no deaths among cattle in the second truckload, which arrived during the period when the 2 calves in the first truckload died. Of the 225 cattle that received antimicrobial treatment, 181 (80.4%) were treated only once and 44 (19.6%) required > 1 treatment.

Serologic examination—Evaluation of geometric mean serum-neutralizing antibody titers to each of the 4 BRDC viruses for all groups revealed a significant increase in the titers to each virus between days 0 and 14 (**Fig 1**). On days 14 to 42, mean antibody titers

Table 1—Morbidity, mortality, and treatment data for 4 truckloads of feedlot cattle that were fed a control diet or a diet supplemented with vitamin E for 7, 14, or 28 days after arrival

Truckload	No. of cattle	Date of arrival	Died		Sick		1 treatment		> 1 treatment	
			No.	%	No.	%	No.	%*	No.	%*
1	85	August 12	2	2.4	56	65.9	45	80.4	11	19.6
2	85	August 20	0	0.0	63	74.1	48	76.2	15	23.8
3	106	December 8	0	0.0	40	37.7	30	75.0	10	25.0
4	111	December 16	0	0.0	66	59.5	58	87.8	8	12.2
Total	**387**	**NA**	**2**	**0.5**	**225**	**58.1**	**181**	**80.4**	**44**	**19.6**

*Represents percentage of sick cattle that were administered the indicated number of antimicrobial treatments because of respiratory tract disease.
NA = Not applicable.

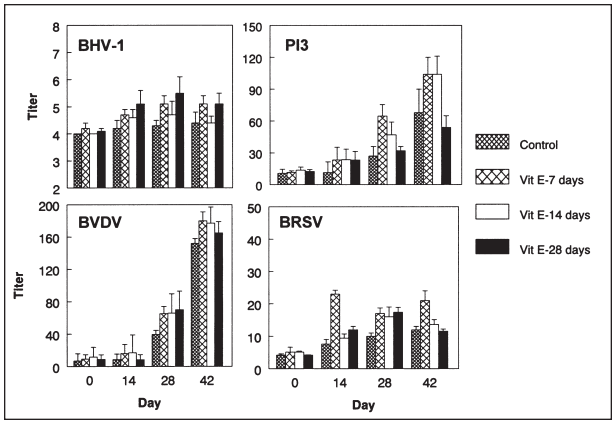

Figure 1—Serum virus-neutralizing antibody responses against 4 viruses for feedlot cattle fed a control diet or a diet supplemented with 2,000 IU of vitamin E for 7, 14, or 28 days. Responses are expressed as geometric mean ± SEM titers. Day 0 = First day on which diets were fed. BHV-1 = Bovine herpesvirus type 1. PI3 = Parainfluenza virus 3. BVDV = Bovine viral diarrhea virus. BRSV = Bovine respiratory syncytial virus.

against the BRDC viruses were frequently higher, but not significantly so, for vitamin E-supplemented cattle, compared with antibody titers for control cattle.

Effects of feeding a vitamin E-supplemented diet—We did not detect significant differences for mean body weights among control or vitamin E dietary groups on days 0 (196.4 to 198.6 kg) or 42 (240.0 to 243.8 kg). Average daily gain (1.02 to 1.06 kg) was not significantly different among the various groups (**Table 2**). However, there was a pattern for fewer sick cattle and fewer treatments because of respiratory tract disease with increased duration of feeding a vitamin E-supplemented diet. This was especially obvious in that 18 cattle in the control group were treated 2 or more times, whereas only 5 cattle in group E28 were treated 2 or more times. Mean treatment cost was significantly (P = 0.02) less for group E28 ($7.44), compared with treatment costs for the control group ($9.23).

On day 0, serum concentrations of acute-phase proteins were not significantly different among any of the vitamin E-supplemented groups or the control group (**Table 3**). Plasma Fib concentrations significantly decreased between days 0 and 7 for all groups.

Serum Hap values significantly decreased between days 7 and 28 for all groups. We did not detect significant differences in Hap concentrations among the vitamin E-supplemented groups and the control group on any of the days on which samples were collected. Although serum Hap concentrations were generally lower for vitamin E-supplemented groups, compared with concentrations for the control group, those values did not differ significantly.

The SAA concentrations decreased, often significantly, between days 0, 7, and 28 for all groups. Consumption of a vitamin E-supplemented diet was associated with significant reductions in SAA concentrations on day 7 for all vitamin E dietary groups, compared with the concentration for the control group. On day 28, SAA concentrations were significantly lower for group E7, compared with concentrations for the other groups.

Between days 0 and 7, serum AGP concentrations increased for all groups; those concentrations were significantly increased for the control group. Increases in AGP concentration were significantly lower in all of the vitamin E-supplemented groups on day 7, compared with concentrations for the control group, whereas on day 28, AGP concentration for the control group was significantly greater than concentrations for groups E7 or E14.

Acute-phase protein responses associated with antimicrobial treatments—On day 0, plasma Fib concentrations were significantly higher for calves that did not subsequently require treatment or calves that were treated more than once, compared with concentrations in calves that were treated only once (**Table 4**). On day 7, calves treated only once had significantly higher plasma Fib concentrations than did calves that were treated more than once or calves that were not treated. The Fib concentration and number of treatments were not significantly correlated (r = 0.05 to 0.08) for any day on which samples were collected.

On days 0 and 7, serum Hap concentrations were significantly higher in calves that were treated more than once for respiratory tract disease, compared with those that were not treated or those that were treated only once. A significant correlation was detected between high Hap concentrations and the number of treatments on day 0 (r = 0.35; P = 0.003) but not on day 7 (r = 0.20; P = 0.08) or 28 (r = –0.11; P = 0.36).

For SAA and serum AGP concentrations, we did not detect significant differences among treatment groups for any days on which samples were collected.

Table 2—Variables regarding production and treatment from groups of feedlot cattle fed a control diet or a diet supplemented with 2,000 IU of vitamin E for 7 (group E7), 14 (group E14), or 28 (group E28) days after arrival at the feedlot

Group	No. of cattle	Mean ± SD average daily gain (kg)	Died		Sick		1 treatment		2 treatments		≥ 3 treatments		Mean ± SD cost of treatment ($)
			No.	%	No.	%	No.	%*	No.	%*	No.	%*	
Control	98	1.02 ± 0.62	2	2.0	64	65.3	46	71.8	15	23.4	3	4.6	9.23 ± 5.87[a]
E7	98	1.06 ± 0.38	0	0.0	60	61.2	48	81.7	9	13.3	3	5.0	8.64 ± 5.27
E14	97	1.05 ± 0.31	0	0.0	53	54.6	44	83.0	8	25.0	1	1.9	8.08 ± 4.13
E28	94	1.05 ± 0.36	0	0.0	48	51.1	43	89.6	5	10.4	0	0.0	7.44 ± 3.19[b]
Total	**387**	**NA**	**2**	**0.5**	**225**	**58.1**	**181**	**80.4**	**37**	**16.4**	**7**	**3.1**	**NA**

[a,b]Values with different superscript letters differ significantly ($P = 0.02$).
See Table 1 for remainder of key.

Table 3—Mean ± SEM plasma or serum concentrations of acute-phase proteins in feedlot cattle fed a control diet or a diet supplemented with 2,000 IU of vitamin E for 7, 14, or 28 days

Acute-phase protein	Day 0*	Day 7	Day 28
Fibrinogen (mg/dl)			
Control	665.7 ± 39.8[A]	239.5 ± 39.3†[B]	346.3 ± 58.2[B]
E7	631.0 ± 46.2[A]	231.4 ± 35.8†[B]	249.7 ± 31.1[B]
E14	775.4 ± 75.2[A]	252.4 ± 34.5†[B]	247.3 ± 25.9[B]
E28	613.1 ± 66.0[A]	223.0 ± 32.7†[B]	215.0 ± 24.0[B]
Haptoglobin (μg/ml)			
Control	401.2 ± 80.6[A]	512.5 ± 106.9[A]	142.2 ± 56.5[B]
E7	383.9 ± 65.8[A]	468.7 ± 97.2[A]	32.5 ± 41.0[B]
E14	396.2 ± 82.0[A]	403.2 ± 118.6[A]	51.6 ± 40.0[B]
E28	278.3 ± 71.9[A]	397.0 ± 109.0[A]	33.9 ± 26.4[B]
Amyloid-A (μg/ml)			
Control	24.9 ± 2.1[A]	19.3 ± 2.4[a,B]	12.0 ± 2.3[a,C]
E7	26.5 ± 1.8[A]	13.7 ± 2.0[b,B]	5.8 ± 1.8[b,C]
E14	25.7 ± 1.6[A]	10.9 ± 1.8[b,B]	7.5 ± 1.7[a,b,B]
E28	20.9 ± 2.2[A]	11.4 ± 2.4[b,B]	7.1 ± 1.7[a,b,B]
α-1-acid glycoprotein (mg/ml)			
Control	587.9 ± 57.8[A]	931.0 ± 80.7[a,B]	802.6 ± 88.1[a,B]
E7	607.5 ± 60.9	715.4 ± 87.9[b]	565.2 ± 75.1[b]
E14	548.0 ± 66.4	696.6 ± 85.0[b]	584.2 ± 69.9[b]
E28	525.8 ± 53.6	562.2 ± 52.7[b]	604.5 ± 56.5[a,b]

*Day 0 = First day on which cattle were fed the diets. †Values for day 7 represent values obtained on day 14.
[a,b,c]Within a column for each variable, means with different superscript lowercase letters differ significantly ($P < 0.05$). [A,B,C]Within a row, means with different superscript uppercase letters differ significantly ($P < 0.05$).

Serum SAA concentrations significantly decreased between days 0, 7, and 28 for calves treated once or more than once. Serum AGP concentrations significantly increased between days 0 and 7 for calves treated once or more than once, but serum concentrations of AGP significantly decreased between days 7 and 28 for calves treated more then once. We did not detect significant correlations (r = –0.15 to 0.08) between AGP or SAA concentrations and number of treatments for any day on which samples were collected.

Values for Hap:SAA were calculated and evaluated as described by Alsemgeest et al,[23] who indicated that predictability of severity of disease was greater when such a ratio was calculated, compared with assessment of the concentration of either acute-phase protein alone. The Hap:SAA values were lower, but not significantly so, on days 0 and 7 for calves that did not develop respiratory tract disease, compared with values for calves treated once or more than once. The Hap:SAA values significantly increased between days 0 and 7 for treated calves. A significant correlation was detected between high Hap:SAA values and number of treatments on day

Table 4—Mean ± SEM plasma or serum concentrations of acute-phase proteins in feedlot cattle fed a control diet or a diet supplemented with 2,000 IU of vitamin E on the basis of number of antimicrobial treatments administered because of respiratory tract disease

Acute-phase protein	No. of treatments	Day 0*	Day 7	Day 28
Fibrinogen (mg/dl)				
	0	883.1 ± 48.4[a]	219.8 ± 31.1†[a]	258.2 ± 22.6
	1	528.0 ± 39.4[b]	271.2 ± 25.3†[b]	246.8 ± 18.3
	> 1	613.6 ± 81.2[a]	145.2 ± 52.9†[a]	197.5 ± 39.5
Haptoglobin (μg/ml)				
	0	108.1 ± 71.7[a]	391.4 ± 195.6[a,b]	203.1 ± 166.7
	1	453.6 ± 49.8[a,A]	493.9 ± 69.8[a,A]	107.8 ± 34.7[B]
	> 1	803.0 ± 103.6[b,A]	852.0 ± 195.5[b,A]	27.0 ± 46.0[B]
Amyloid-A (μg/ml)				
	0	26.4 ± 8.3	8.2 ± 1.3	9.0 ± 3.4
	1	24.6 ± 1.2[A]	14.4 ± 1.5[B]	8.7 ± 1.3[C]
	> 1	29.6 ± 1.9[A]	13.0 ± 2.9[B]	3.4 ± 1.5[C]
α-1-acid glycoprotein (μg/ml)				
	0	380.2 ± 208.5	523.6 ± 165.9	713.6 ± 344.7
	1	603.6 ± 40.7[A]	757.7 ± 54.6[B]	662.9 ± 43.6[A,B]
	> 1	561.6 ± 60.9[A]	857.6 ± 132.9[B]	464.6 ± 71.0[A]
Haptoglobin: Amyloid-A				
	0	8.4 ± 1.8	40.7 ± 17.5	17.7 ± 11.2
	1	18.2 ± 2.4[A]	50.4 ± 8.3[B]	8.9 ± 3.4[A]
	> 1	25.7 ± 4.2[A]	73.1 ± 22.2[B]	3.6 ± 6.5[A]

See Table 3 for key.

Table 5—Mean ± SEM plasma or serum concentrations of acute-phase proteins determined on the initial day that cattle were treated because of respiratory tract disease and 14 days after treatment, on the basis of number of treatments administered

Acute-phase protein	No. of treatments	Initial	14 days after
Fibrinogen (mg/dl)			
	1	582.4 ± 24.4[A]	331.1 ± 17.9[B]
	> 1	643.3 ± 53.8[A]	380.5 ± 58.0[B]
Haptoglobin (μg/ml)			
	1	553.7 ± 54.3[a,A]	190.7 ± 50.6[B]
	> 1	765.5 ± 61.8[b,A]	111.6 ± 52.8[B]
Amyloid-A (μg/ml)			
	1	24.7 ± 0.9[A]	10.0 ± 1.0[a,B]
	> 1	26.2 ± 2.1[A]	5.1 ± 1.3[b,B]
α-1-acid glycoprotein (mg/ml)			
	1	633.6 ± 32.3[A]	546.5 ± 24.7[B]
	> 1	619.9 ± 55.2	497.5 ± 42.1

See Table 3 for key.

0 (r = 0.27) but not on days 7 (r = –0.054) and 28 (r = 0.10).

Acute-phase protein responses on the day calves first received antimicrobial treatment and 2 weeks later—All treated cattle had significantly lower serum concentrations of Fib, Hap, and SAA 14 days after antimicrobial treatment, compared with concentrations at the time of the initial antimicrobial treatment (**Table 5**). Serum AGP concentrations also decreased between the time of the first antimicrobial treatment and 14 days after treatment; however, only concentrations for calves treated once differed significantly. At the time of the first antimicrobial treatment, serum Hap concentrations were significantly lower for calves that responded favorably to 1 treatment, compared with concentrations for calves that required > 1 treatment. Concentrations of SAA were significantly lower 14 days after antimicrobial treatment for calves that received > 1 treatment, compared with concentrations of calves that were treated only once.

Discussion

Analysis of results of the study reported here indicated that vitamin E supplementation of diets fed to newly arrived cattle at feedlots did not influence weight gain; however, mean treatment cost decreased for those calves receiving a vitamin E-supplemented diet for 28 days. The mechanism by which vitamin E could be associated with reduced treatment costs is not known; however, vitamin E is known for its antioxidant function and can augment immunity through enhanced glutathione peroxidase activity in leukocytes and stimulation of helper T cells, chemotaxis, phagocytosis, and antibody production.[25] Droke and Loerch[26] documented that performance or health status of cattle injected with selenium and vitamin E at the time of arrival in a feedlot did not differ from that of control cattle. Injection of selenium and vitamin E, however, did stimulate higher antibody responses to *M haemolytica* vaccination, suggesting an immunostimulant role for the injected compounds. In the study reported here, cattle fed a vitamin E-supplemented diet often had higher antibody titers in response to vaccination against BRDC viruses, but not significantly so, than did vaccinated cattle fed the control diet. In addition, animals deficient in vitamin E and selenium are more susceptible to infections. Beck and Levander[27] reported that laboratory animals deficient in vitamin E and selenium were susceptible to a normally nonlethal viral infection. They postulated that oxidative stress on the host enhanced susceptibility of animals to viral infection. It is not known whether cattle in the study reported here were deficient in vitamin E or selenium at the time of arrival at the feedlot or whether stress of transportation could have created oxidative stress. Either stress condition may have allowed vitamin E supplementation to enhance resistance to infectious agents or augment immune responsiveness, thus reducing treatment costs.

Analysis of the study reported here indicated that feeding of vitamin E-supplemented diets to newly arrived calves was associated with reduced serum acute-phase protein concentrations on day 7 for SAA and AGP and day 28 for Hap, SAA, and AGP, compared with serum concentrations for control calves. It is likely that vitamin E supplementation decreased inflammatory mediators such as interleukin-6 and tumor necrosis factor-α, which stimulate the acute-phase response through reduction of oxidative stress. In humans, vitamin E supplementation significantly decrease the production of C-reactive protein, another acute-phase protein, in diabetics and nondiabetics and minimize other aspects of the acute-phase response and inflammatory damage involved in people with atherosclerosis.[28] Whether it is desirable to reduce the acute-phase response of stressed cattle must be questioned. For example, Hap is biosynthesized in the liver as well as adipose tissue and the lungs, and Hap provides antioxidant and antimicrobial activity and plays a role in stimulation of angiogenesis.[29] Therefore, during development of respiratory tract disease, the acute-phase response is probably important in helping an animal resist respiratory tract pathogens.

In this study, we examined Fib, Hap, SAA, and AGP concentrations as potential markers for severity of disease. Plasma Fib concentrations have traditionally been used to assess clinical illness in cattle.[24] The plasma Fib assay is easy to perform, and assay results can be obtained rapidly. However, on day 0 in this study, mean Fib concentrations were significantly higher in calves that were not subsequently diagnosed with BRDC than were concentrations for calves that required antimicrobial treatment. Those findings are opposite to the expectations for an acute-phase protein; therefore, results of the Fib assay did not appear to be a useful prognostic or diagnostic tool for monitoring respiratory tract disease and treatment in these cattle.

Numerous studies[5,10,20,22,23] have been conducted on the use of acute-phase protein responses to predict severity or chronicity of sick cattle. Alsemgeest et al[23] indicated that serum Hap and SAA concentrations as well as Hap:SAA values are increased in cattle with inflammatory diseases and that serum Hap concentrations and Hap:SAA values are significantly increased in cattle with chronic, rather than acute, inflammation. In contrast, Horadagoda et al[20] found that Hap, SAA, and AGP concentrations are significantly greater in cattle with acute, compared with chronic, inflammation. Because those studies examined a large number of inflammatory diseases, their results may not be comparable to those found in the study reported here. More appropriate to our study, Godson et al[3] found that serum Hap concentrations correspond to the severity of respiratory tract disease in calves inoculated with BHV-1 and *M haemolytica*. Heegaard et al[30] found that the magnitude and duration of serum Hap concentration correlated well with the severity of experimentally induced BRSV infection, whereas serum SAA concentrations increased most rapidly following infection. On days 0 and 7 in the study reported here, serum Hap concentrations were significantly lower for cattle that did not become ill or responded to 1 antimicrobial treatment, compared with concentrations in calves that required > 1 antimicrobial treatment. In addition,

serum Hap concentrations on day 0 correlated with the number of treatments required. Serum AGP and Hap:SAA values were generally lower, but not significantly so, on days 0 and 7 for calves that did not become ill, compared with results for calves that required 1 or more treatments. Although it is assumed that clinically ill calves in our study had acute onset of disease, SAA and AGP concentrations failed to discriminate between those that became ill and those that did not on any of the days on which samples were collected. Therefore, for this model of BRDC, serum Hap concentrations were potentially the most useful in predicting respiratory tract disease and response to treatment.

Young et al[5] documented that after 65 days of feeding, cattle with higher serum Hap concentrations had a significantly higher percentage of clinical respiratory tract disease than did cattle with low serum Hap concentrations. In another study,[22] feedlot cattle with clinical respiratory tract disease that were treated with antimicrobials had significantly lower Hap concentrations, compared with Hap concentrations in sick cattle not treated with antibiotics. In the study reported here, at time of initial antimicrobial treatment, calves that required only 1 treatment had serum Hap concentrations that were significantly less than concentrations in calves that required > 1 treatment. Fourteen days after completion of successful treatment, Hap concentrations were not significantly different between these 2 groups of calves. Therefore, in addition to Hap concentrations being reduced following antimicrobial treatment, serum Hap concentrations may also be useful for predicting the severity of disease, likelihood of a chronic disease state, and necessity for multiple treatments.

In contrast to the findings of Alsemgeest et al,[23] the reliability of the predictions derived from the Hap:SAA values was less than for serum Hap concentrations alone. Therefore, the most practical determination to use for the development of a prognostic tool is serum Hap concentration. Results obtained from the commercial Hap radial immunodiffusion test in the study reported here were generally consistent with those of other studies, and our results had consistent patterns relative to clinical determination of respiratory tract disease in our calves. The other acute-phase proteins measured in this study did not appear useful in monitoring recovery from or the efficacy of treatment for naturally acquired BRDC.

[a]BRSV-Vac 4, Diamond Scientific Co, Ames, Iowa.
[b]Vision7, Intervet, Millsboro, Del.
[c]Ivomec-Plus, Merial, Woodbridge, NJ.
[d]Micotil, Elanco, Indianapolis, Ind.
[e]Nuflor, Schering Plough Animal Health, Kenilworth, NJ.
[f]Excenel, Pharmacia-Upjohn, Kalamazoo, Mich.
[g]Bovine Hp–SRID (P0105-1), Cardiotech Services Inc, Louisville, Ky.
[h]Tridelta Phase range kit, Tri-Delta Development Ltd, Wicklow, Ireland.
[i]V Max kinetic microplate reader, Molecular Devices Inc, Sunnyvale, Calif.
[j]Bovine α_1AG–SRID (P0101-1), Cardiotech Services Inc, Louisville, Ky.
[k]Oklahoma Animal Disease Diagnostic Laboratory, Stillwater, Okla.
[l]SAS, version 8.2, SAS Institute Inc, Cary, NC.

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