The Relationship of Oxidative Stress to Bovine Respiratory Disease of Feeder Cattle

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Bovine respiratory disease complex (BRD), also known as "shipping fever", is a major economic concern to the beef cattle industry, with annual losses estimated at $600-700 million. These economic considerations have prompted the investigation of its etiology, treatment, and prevention (Loan, 1984). The defining characteristic of BRD is a stress-related alteration in susceptibility of the bovine respiratory tract to colonization by bacterial and viral pathogens that under normal circumstances present little or no risk to the animal (Babiuk and Acres, 1984). The stress of relocation/shipping can be a precipitating cause of this increased susceptibility (Thomson, 1984). BRD represents a reasonably defined disease model of multifactorial etiology that involves the dominant stressors such as physical (transportation), biological and psychological stress. Furthermore, the model is suitable for investigating synergisms with other biologic and chemical stressors to which cattle are exposed in the beef cattle industry.

The oxidative processes of aerobic organisms, including mitochondrial respiration and oxidative metabolism of endogenous and exogenous chemicals, produce reactive oxygen species (ROS), e.g. superoxide anion, hypochlorous acid, hydrogen peroxide, epoxides hydroxyl radicals and fatty acid radicals. In addition to the normal cellular processes that produce ROS, environmental insults (solar radiation, dust, smoke, certain mycotoxins and nitrates) and inflammatory response also account for a greater proportion of ROS in humans and animals that have to be contained. To protect themselves against oxidant damage, aerobic organisms have evolved elaborate defense systems (Kehrer, 1993). These defenses include enzymes that catalyze the degradation of ROS to prevent tissue damage, general antioxidants to prevent processes of initiation and respiratory burst during phagocytosis.

Although oxidative stress has not been identified as an etiologic factor in BRD, accumulating circumstantial evidence (Table 1) is consistent with its involvement. Acute confinement of calves has been reported to decrease serum ascorbic acid levels (Mason et al., 1984), consistent with its depletion by reaction with ROS. Supplementation of diets with antioxidant vitamin E (800-1600 I.U./hd/day) produced a 12-27% reduction in the incidence of BRD in feeder calves and improved their performance, as measured by average daily weight gain (Hutcheson and Cole, 1985; Hays et al., 1978) and recovery rate from IBR infection (Chirase et al., 1991; 1994). The multifactorial etiology of BRD is also consistent with multiple stressors that produce ROS in an additive or synergistic manner to overwhelm the antioxidant defenses. Furthermore, physical (market stress), psychological, chemical and biological (e.g. vaccination) stressors identified in the etiology of BRD are stressors known to produce ROS. The relationship between oxidative stress and BRD resulting from market stress of beef cattle is not well understood. Our research team (CREET) in collaboration with scientists from Indiana University Medical School, and Dermigen, a private company, initiated some studies to evaluate the relationship of factors (physical/psychological/chemical/biological) precipitating BRD and biological markers of oxidative stress in feeder cattle, and to establish the role of micronutrients (microminerals and vitamins) in the prevention of oxidative stress to further enhance the immune response of beef cattle.

In the first experiment, 108 crossbred steers (average wt 550 lb) were purchased from Tennessee via the normal order buyer system and used to study the effects of marketing stress on biomarkers of oxidative stress. The calves were bled and transported approximately 2,200 km to the Texas Agricultural Experimentation/USDA-ARS beef cattle research facilities in Bushland. Upon arrival at the feedlot, steers were bled again and serum from blood was analyzed for the concentrations of two biomarkers (total antioxidant capacity or TACA and malondialdehyde or MDA) of oxidative stress. Biomarker concentrations before (Tennessee) and after (Texas) shipping were correlated with body weights and rectal temperatures.

Pearson correlation coefficients indicated that cattle with high serum MDA values resulting from marketing stress eventually produce higher ($P<.001$) MDA values during transportation stress ($R^2=.51$), suggesting an additive effect of marketing and transportation stresses. However, there was no relationship between pre- or posttransit serum MDA and TACA concentrations. At the feedlot, as steers continued to exhibit a decrease in body

Table 1. Evidence of ROS involvement in Disease and Immune Function

Item	Modulation Factors
Reactive Oxygen Species (ROS)	*Enzyme (cofactor)*
Superoxide anion	Superoxide dismutase (Copper/Zinc/Manganese)
Hydrogen peroxide	Catalase (Iron)
Hydrogen peroxide	Glutathione peroxidase (Selenium)
Organic peroxides	Glutathione peroxidase (Selenium)
Organic peroxides	Glutathione-S-transferase (Selenium)
Initiation Reactions and Respiratory Burst	
	General Antioxidants (Destroying Agents)
	Glutathione
	Uric acid
	Melatonin
	Hypotaurine
	Carotenoids (Vitamin A)
	Ascorbate (Vitamin C)
	α-tocopherol (Vitamin E)
Cellular/Organelle/Molecules	*Damage Repairing/Cleaning Agents*
	Lipases
	Proteases
	DNA/RNA repair enzymes

Figure 1. Effect of posttransit time (days) on Body weights (lb) of stressed steers

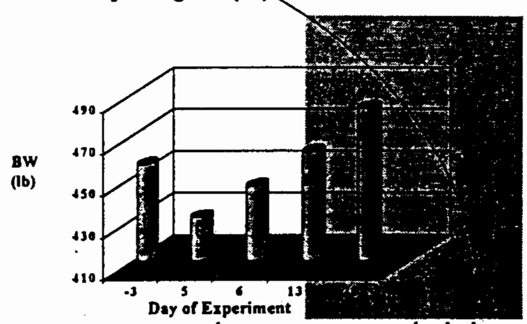
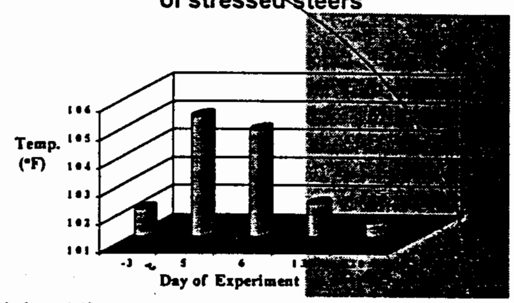


Figure 2. Effect of posttransit time (days) on rectal temperatures of stressed steers



core temperature, there was a gradual increase in body weight (Figures 1&2). However, serum TACA concentrations remained depressed up to and including day 28 which suggests that the steers were still prone to infection (Figure 3).

Preliminary data analysis also indicated that marketing stress significantly reduced ($P<.002$) serum TACA and increased ($P<.0004$) serum MDA concentrations of feeder calves (Table 2). Coffey (1990) reported that the oxidative stress index for bovine was <6 IU/mL of MDA in whole blood. Using this index as the baseline value for nonstressed steers, the process of purchasing calves via order buyer barn alone increased lipid peroxidation in these calves by 82% and compounded by an additional increase of 220% (Table 2) from shipping stress. These data suggests that biological markers of stress could be used to access the health status of feeder calves. Additional studies are planned to correlate these biomarkers with BRD scores and to apply stressors such as feedlot dust and vaccination practices to further understand these relationships. Also, future research will measure leukocyte DNA concentrations and used to evaluate the genetic bases of oxidative stress and BRD in feeder cattle.

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Table 2. Effect of marketing stress on rectal temperature and serum biomarkers of oxidative stress of feeder cattle.

Item ug/ml	Rectal Temperature, °F	TACA, IU/ml	MDA,
Number	108	108	108
Tennessee	102[a]	4409[c]	10.93[e]
Texas	105[b]	4000[d]	30.24[f]
SE	1.2	76	3.40

[ab]Column means differ ($P<.05$).
[cd]Column means differ ($P<.002$).
[ef]Column means differ ($P<.0004$).

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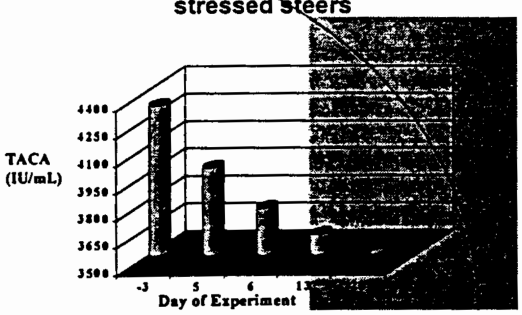
Figure 3. Effect of posttransit time (days) on serum TACA (IU/mL) of stressed steers



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