

2012

Effect of Oral Meloxicam on Health and Performance of Beef Steers Relative to Bulls Castrated on Arrival at the Feedlot

Johann F. Coetzee

Iowa State University, hcoetzee@iastate.edu

L. N. Edwards

Kansas State University

Gretchen A. Mosher Dr.

Iowa State University, gamosher@iastate.edu

N. M. Bello

Kansas State University

Annette M. O'Connor

Follow this and additional works at: http://lib.dr.iastate.edu/vdpam_pubs

Iowa State University, oconnor@iastate.edu

 Part of the [Animal Studies Commons](#), [Large or Food Animal and Equine Medicine Commons](#),
See next page for additional authors
and the [Veterinary Toxicology and Pharmacology Commons](#)

The complete bibliographic information for this item can be found at http://lib.dr.iastate.edu/vdpam_pubs/28. For information on how to cite this item, please visit <http://lib.dr.iastate.edu/howtocite.html>.

This Article is brought to you for free and open access by the Veterinary Diagnostic and Production Animal Medicine at Iowa State University Digital Repository. It has been accepted for inclusion in Veterinary Diagnostic and Production Animal Medicine Publications by an authorized administrator of Iowa State University Digital Repository. For more information, please contact digirep@iastate.edu.

Effect of Oral Meloxicam on Health and Performance of Beef Steers Relative to Bulls Castrated on Arrival at the Feedlot

Abstract

Castration in weaned calves is stressful and affects profitability by reducing ADG and increasing susceptibility to disease. This study evaluated the effect of meloxicam, a nonsteroidal anti-inflammatory drug (NSAID), on performance and health of calves received as steers compared with bull calves surgically castrated on arrival at the feedlot. British × Continental bulls (n = 145) and steers (n = 113; BW = 193 to 285 kg) were transported for 12 h in 3 truckloads (d 0), weighed, and randomly assigned to receive either lactose placebo (CONT; 1 mg/kg) or meloxicam (MEL; 1 mg/kg) suspended in water and administered per os, 24 h before castration. On d 1, bulls were surgically castrated (CAST) and steers were processed without castration (STR). Combinations of CONT/MEL and CAST/STR were allocated to 24 pens (6 pens per treatment) of 8 to 14 calves each. Pen was the experimental unit. Plasma meloxicam concentrations at the time of castration (d 1) were determined by HPLC-mass spectroscopy. Pen-level ADG, DMI, and G:F were estimated using BW obtained on d 0, 14, and 28 and weigh-back of feed. Individual animals were classified as sick based on a depression score of ≥2 on a 5-point scale and a rectal temperature of ≥39.8°C. On d 0, 1, and 14, calf chute temperament was evaluated using a 4-point scale. Data were analyzed using generalized linear mixed models and survival curve analyses. Castration reduced pen ADG ($P < 0.001$) and G:F ($P < 0.001$) from d 1 to 14, yet no effects ($P > 0.45$) were apparent by d 28. For all treatment groups, DMI increased with days on feed ($P < 0.0001$) but was less in CAST compared with STR calves ($P < 0.016$) throughout the study. From d 15 to 28, ADG increased ($P = 0.0011$) in CAST but not STR calves, and G:F decreased ($P = 0.0004$) in STR but not CAST calves. In CAST calves only, MEL treatment reduced the pen-level first pull rate ($P = 0.04$) and reduced bovine respiratory disease morbidity rate ($P = 0.03$). The frequency of chute escape behavior was greater on arrival and at castration in CAST vs. STR calves ($P < 0.01$) but not significantly different at d 14 ($P = 0.22$). Mean MEL concentrations at castration were no different between treated STR and CAST calves ($P = 0.70$). Meloxicam administration before castration in postweaning calves reduced the incidence of respiratory disease at the feedlot. These findings have implications for developing NSAID protocols for use in calves at castration with respect to addressing animal health and welfare concerns.

Keywords

animal welfare, castration, cattle, health, meloxicam, performance

Disciplines

Animal Studies | Large or Food Animal and Equine Medicine | Veterinary Toxicology and Pharmacology

Comments

This article is from *Journal of Animal Science* 90 (2012): 1026, doi:[10.2527/jas.2011-4068](https://doi.org/10.2527/jas.2011-4068). Posted with permission.

Authors

Johann F. Coetzee, L. N. Edwards, Gretchen A. Mosher Dr., N. M. Bello, Annette M. O'Connor, Bing Wang, Butch Kukanich, and D. A. Blasi

Effect of oral meloxicam on health and performance of beef steers relative to bulls castrated on arrival at the feedlot¹

J. F. Coetzee,*² L. N. Edwards,† R. A. Mosher,* N. M. Bello,‡ A. M. O'Connor,§
B. Wang,§ B. KuKanich,# and D. A. Blasi†

*Department of Clinical Sciences, College of Veterinary Medicine, †Department of Animal Sciences and Industry, College of Agriculture, and ‡Department of Statistics, College of Arts and Sciences, Kansas State University, Manhattan 66506; §Veterinary Diagnostic and Production Animal Medicine, College of Veterinary Medicine, Iowa State University, Ames 50011; and #Department of Anatomy and Physiology, College of Veterinary Medicine, Kansas State University, Manhattan 66506

ABSTRACT: Castration in weaned calves is stressful and affects profitability by reducing ADG and increasing susceptibility to disease. This study evaluated the effect of meloxicam, a nonsteroidal anti-inflammatory drug (NSAID), on performance and health of calves received as steers compared with bull calves surgically castrated on arrival at the feedlot. British × Continental bulls (n = 145) and steers (n = 113; BW = 193 to 285 kg) were transported for 12 h in 3 truckloads (d 0), weighed, and randomly assigned to receive either lactose placebo (CONT; 1 mg/kg) or meloxicam (MEL; 1 mg/kg) suspended in water and administered per os, 24 h before castration. On d 1, bulls were surgically castrated (CAST) and steers were processed without castration (STR). Combinations of CONT/MEL and CAST/STR were allocated to 24 pens (6 pens per treatment) of 8 to 14 calves each. Pen was the experimental unit. Plasma meloxicam concentrations at the time of castration (d 1) were determined by HPLC-mass spectroscopy. Pen-level ADG, DMI, and G:F were estimated using BW obtained on d 0, 14, and 28 and weigh-back of feed. Individual animals were classified as sick based on a depression score of ≥ 2 on a 5-point scale and a rectal temperature of $\geq 39.8^\circ\text{C}$. On d 0, 1, and 14, calf chute

temperament was evaluated using a 4-point scale. Data were analyzed using generalized linear mixed models and survival curve analyses. Castration reduced pen ADG ($P < 0.001$) and G:F ($P < 0.001$) from d 1 to 14, yet no effects ($P > 0.45$) were apparent by d 28. For all treatment groups, DMI increased with days on feed ($P < 0.0001$) but was less in CAST compared with STR calves ($P < 0.016$) throughout the study. From d 15 to 28, ADG increased ($P = 0.0011$) in CAST but not STR calves, and G:F decreased ($P = 0.0004$) in STR but not CAST calves. In CAST calves only, MEL treatment reduced the pen-level first pull rate ($P = 0.04$) and reduced bovine respiratory disease morbidity rate ($P = 0.03$). The frequency of chute escape behavior was greater on arrival and at castration in CAST vs. STR calves ($P < 0.01$) but not significantly different at d 14 ($P = 0.22$). Mean MEL concentrations at castration were no different between treated STR and CAST calves ($P = 0.70$). Meloxicam administration before castration in postweaning calves reduced the incidence of respiratory disease at the feedlot. These findings have implications for developing NSAID protocols for use in calves at castration with respect to addressing animal health and welfare concerns.

Key words: animal welfare, castration, cattle, health, meloxicam, performance

©2012 American Society of Animal Science. All rights reserved.

J. Anim. Sci. 2012. 90:1026–1039
<http://dx.doi.org/10.2527/jas.2011-4068>

¹This project was supported by Agriculture and Food Research Initiative Competitive grant number 2008-35204-19238 from the USDA National Institute of Food and Agriculture (Washington, DC) and the American Association of Bovine Practitioners (Auburn, AL). The authors acknowledge the Kansas State University Beef Stocker Unit for collecting and providing the data used in this research. Special thanks go to Marc Epp, research assistant and manager of the

Beef Stocker Unit, for his assistance with these data. Contribution number 11-278-J from the Kansas Agricultural Experiment Station. A provisional patent application (PCT/US2011/044017) was filed on July 14, 2011.

²Corresponding author: hcoetzee@iastate.edu

Received March 16, 2011.

Accepted September 27, 2011.

INTRODUCTION

Castration of bulls intended for beef production is a common livestock management procedure in the United States (USDA NASS, 2011). Benefits of castration include improved meat quality and fewer injuries in confinement operations. Nevertheless, castration post-weaning affects profitability by decreasing ADG and increasing susceptibility to bovine respiratory disease (BRD; Massey et al., 2011). Although castration is considered painful, it is typically performed without analgesia (Coetzee et al., 2010). Calls for routine analgesic use at castration are increasing due to growing public concern about animal welfare (Weary and Fraser, 2004). Currently, no compounds are approved for pain relief in cattle and available products may not be practical or economical for routine use because drug costs are not offset by health or performance benefits (Booker et al., 2009; Coetzee et al., 2010). Identification of analgesic compounds that may also have performance benefits after castration would provide livestock producers with an efficient and economically viable way to address animal health and welfare concerns.

Previous studies support the hypothesis that extended exposure to a nonsteroidal anti-inflammatory drug (NSAID) may reduce stress and improve performance after castration. For example, the NSAID sodium salicylate administered in drinking water for 2 d after dehorning and castration reduced serum cortisol after surgery and improved ADG over 13 d (Baldrige et al., 2011). Meloxicam is an NSAID that is approved in Canada for pain relief after disbudding in calves. The mean bioavailability of meloxicam after oral administration of 1 mg/kg is 100%, and the plasma elimination half-life in ruminant calves is 27 h (Coetzee et al., 2009). This suggests that the effects of meloxicam may last several days after a single treatment. The objective of this study was to investigate the effect of oral meloxicam administration on performance and health of steers and bulls after surgical castration.

MATERIALS AND METHODS

Before the initiation of this experiment, all animal use, handling, and sampling techniques described herein were approved by the Kansas State University Animal Care and Use Committee.

Animals, Housing, Treatment Allocation, and Processing

This study was designed as a stratified 2-arm parallel trial. The strata were calves received as steers (STR) vs. calves castrated on arrival (CAST), and the drug treatment was meloxicam (MEL) or placebo (CONT; Figure 1). Two hundred fifty-eight medium-large frame, polled, Continental × British or British crossbred bull (CAST; n = 145) and steer (STR; n = 113) calves aged 8 to 10 mo and weighing 193 to 285 kg were procured

from sale barns in southeastern Tennessee. Calves were shipped approximately 1,086 km to the Kansas State University Beef Stocker Unit outside Manhattan, where they were housed for the duration of the study. Calves were maintained in open pens that consisted of a combination of concrete aprons and dirt pens. Each pen was 192 m² with an allowance of approximately 14 to 24 m²/animal with 12 m of bunk space and 1 water source per pen. A maximum of 14 animals/pen was allowed. Calves arrived at the unit during a 2-wk period in March 2010 in 3 loads (lots) of mixed gonadal status carrying 83, 87, and 88 calves, respectively. On arrival, calves were unloaded and sorted (d 0).

During sorting, calves were individually weighed and given an individual identification tag in the right ear. A tissue sample for bovine viral diarrhea (BVD) analysis was taken from the left ear using a specialized ear notch device (Caisley International GmbH, Bocholt, Germany). Ear notch samples were analyzed by antigen capture ELISA at the Kansas State University Veterinary Diagnostic Laboratory. All calves were confirmed negative for BVD virus. Calves were determined to be bulls or steers by palpation and were then randomly assigned to either a MEL or CONT-treated group by a randomization table generated using Excel (Microsoft Corp., Redmond, WA). A total of 71 bulls (MEL-CAST) and 58 steers (MEL-STR) were scheduled to receive meloxicam, whereas 74 bulls (CONT-CAST) and 55 steers (CONT-STR) were scheduled to receive treatment with the placebo. All steers were assigned to STR, namely the uncastrated group, and all bulls were allotted to the surgical castration group, CAST. After ranking the animals by BW, treatment groups, defined as the combination of CONT/MEL and CAST/STR, were allocated to 24 pens (6 pens per treatment) of 8 to 14 calves each, such that pen was recognized as the experimental unit.

Meloxicam tablets [Meloxicam tablets USP 15 mg (NDC 29300-125-01), Unichem Pharmaceuticals USA Inc., Rochelle Park, NJ; lot #GMMH09021] were administered at 1 mg of meloxicam/kg of BW per os (PO). The dose was rounded down to the nearest whole tablet so that no animal received a dose exceeding 1 mg/kg. Calves in the placebo-treated group received an equivalent dose of D(+)-lactose monohydrate (Fluka Analytical, Buchs, Germany), a pharmacologically inactive excipient used in the manufacture of meloxicam tablets, PO. The doses were calculated using arrival BW and were administered by suspending crushed meloxicam tablets or placebo in approximately 50 mL of water and delivering this orally with a dosing syringe within 30 s of suspension.

Approximately 24 h after the dosing (d 1), calves were brought back through the processing chute and given a commercial modified-live, viral respiratory vaccine containing infectious bovine rhinotracheitis virus; parainfluenzavirus-3; bovine viral diarrhea virus; bovine respiratory syncytial virus; *Mannheimia haemolytica* (Pyramid 5+ Presponse SQ, Fort Dodge Animal

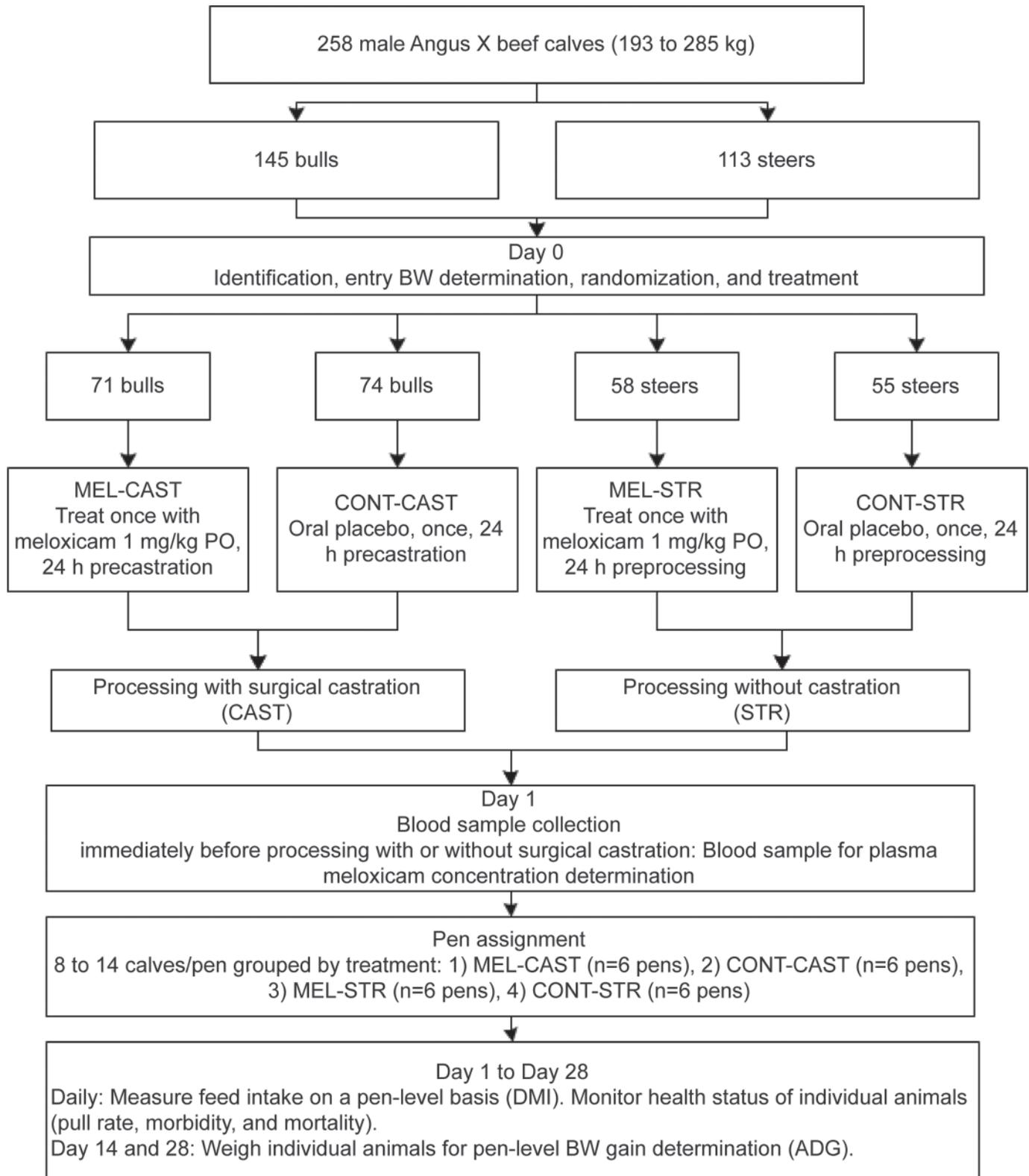


Figure 1. Study outline representing timeline for calves administered lactose placebo (CONT; 1 mg/kg) or meloxicam (MEL; 1 mg/kg, Unichem Pharmaceuticals USA Inc., Rochelle Park, NJ) suspended in water per os, 24 h before castration. On d 1, bulls were surgically castrated (CAST) and steers were processed without castration (STR).

Health, Wyeth, Madison, NJ); a multivalent clostridial vaccine (Calvary 9, Intervet/Schering-Plough Animal Health, Boxmeer, the Netherlands); injectable ivermectin at 200 μ g/kg of BW (Ivomec, Merial Ltd., Duluth,

GA); and a metaphylactic antimicrobial, ceftiofur crystalline free acid at 6.6 mg/kg of BW (Excede, Pfizer Animal Health, New York, NY). Products were administered according to label instructions.

Additionally on d 1, castration was performed using open surgical technique without administration of a local anesthetic, consistent with standard industry practice in the United States (Coetzee et al., 2010). Briefly, the scrotum of each calf was cleaned with dilute chlorohexidine disinfectant and incised longitudinally with a Newberry knife (Jorgensen Lab, Loveland, CO). The testes and spermatic cords were exteriorized by blunt dissection, and the cremaster was broken using manual traction. The spermatic cords were cut using a White's Double Crush emasculator (Jorgensen Lab) applied for approximately 30 s. Steers were subjected to the same handling procedures apart from knife cutting and castration. Processing and surgical castration was performed by the same operator to minimize variation in procedure. After processing, calves were sorted into study pens.

Calves were reweighed on d 14. Additionally, calves were revaccinated with the viral respiratory vaccine (Pyramid 5+ Presponse SQ, Fort Dodge Animal Health, Wyeth) and given a pour-on eprinomectin at 500 µg/kg of BW (Eprinex, Merial Ltd.) at this time. Final BW was obtained at the end of the study on d 28.

Collection of Samples

Blood samples to confirm meloxicam dosage were obtained on d 1 via jugular venipuncture immediately after processing. Blood also was collected from the placebo-treated calves to maintain equality between study groups and to ensure that personnel remained masked to drug treatment group. Blood samples were collected in 6-mL evacuated tubes that contained lithium heparin (Vacuette plasma tubes, Greiner Bio-One, Monroe, NC) and stored on ice for up to 2 h before processing. Blood samples were centrifuged for 10 min at $1,500 \times g$ at 4°C. Plasma was then harvested, placed in cryovials, and frozen at -70°C until analysis. All samples from MEL-treated calves were analyzed within 60 d after sample collection.

Plasma Meloxicam Analysis

Plasma concentrations of meloxicam (mass:charge ratio [m/z] 352.09→114.90) were determined with HPLC (Shimadzu Prominence, Shimadzu Scientific Instruments, Columbia, MD) and mass spectrometry (API 2000, Applied Biosystems, Foster City, CA). Plasma samples or standards (100 µL) were added to 100 µL of internal standard (piroxicam 0.5 µg/mL in methanol, m/z 332.12→95.10) and 300 µL of methanol with 0.1% formic acid to precipitate the proteins. The samples were vortex mixed for 5 s and centrifuged for 10 min at $10,000 \times g$ at 4°C. The supernatant, 200 µL, was transferred to an injection vial with the injection volume set to 10 µL. The mobile phase consisted of A: acetonitrile and B: 0.1% formic acid at a flow rate of 0.4 mL/min. The mobile phase consisted of 85% B from 0 to 0.5 min with a linear gradient to 50% B at 2.5 min, which was

maintained until 3 min, followed by a linear gradient to 85% B at 4 min, with a total run time of 5 min. Separation was achieved with a C8 column (Supelco Discovery C8, 50 mm × 2.1 mm × 5 µm; Sigma-Aldrich, St. Louis, MO) maintained at 40°C. The standard curve was linear from 0.01 to 10 µg/mL and was accepted if the correlation coefficient exceeded 0.99 and predicted values were within 15% of the actual values. The accuracy of the assay was 103% ± 7% of the actual value, and the CV was 7%, determined on replicates of 5 each at 0.025, 0.5, and 5 µg/mL.

Temperament Score

During processing and castration on d 0, 1, and 14, animal temperament in the hydraulic squeeze chute was evaluated by a single observer masked to drug treatment using a 4-point scale (1 = calm, no movement; 2 = restless shifting; 3 = squirming, occasional shaking of the chute; 4 = continuous vigorous movement and shaking of the chute, rearing, twisting, and struggling; Voisinet et al., 1997). At each time, animals received a single temperament score.

Nutrition Program

Dietary composition is reported on a DM basis. The arrival diet consisted of prairie hay containing 7.0% CP and 0.44 Mcal of NE_g/kg of DM. Beginning 1 d after arrival, the calves were fed a total mixed ration (**TMR**) consisting of prairie hay, alfalfa hay, dry rolled corn, wet corn gluten feed, and a commercial premix pellet (Cargill Animal Nutrition, Minneapolis, MN). The percentage of each ingredient in the diets on an as-fed basis is presented in Table 1. This ration was formulated to contain 15.2% CP and 1.09 Mcal of NE_g/kg of DM. Beginning 8 d postarrival and continuing through d 18, calves were fed a TMR incorporating the same ingredients as above, but containing 15.2% CP and 1.14 Mcal of NE_g/kg of DM. On d 19 and continuing through the study endpoint, calves were fed a TMR utilizing the same ingredients formulated to contain 14.4% CP and 1.20 Mcal of NE_g/kg of DM. Daily feed allowances to each pen were recorded. Water was provided for ad libitum intake. Feed bunks were evaluated twice daily, and the weight of feed not consumed was used as a basis for the amount delivered at the next feeding.

Health Program

Kansas State University Beef Stocker Unit personnel conducted twice daily evaluations of the cattle and were masked to drug treatment assignment throughout the study. Animals were deemed sick based on subjective criteria including general appearance and attitude, gauntness, and reluctance to move. If a sick calf was identified, it was removed from the pen, brought to the processing unit, and its rectal temperature was obtained.

Table 1. Dietary components of the rations fed in the study (% , as fed)

DOF ¹	Supplement ²	Dry-rolled corn	WCGF ³	Prairie hay	Alfalfa hay
1 to 7	3	28	30	16	23
8 to 18	3	29	37	16	15
19 to 28	3	36	37	15	9

¹DOF: days on feed.

²Supplement contains 600 g/t of monensin (Elanco Animal Health, Greenfield, IN).

³Wet gluten feed (Sweetbran, Cargill Animal Nutrition, Minneapolis, MN).

To be considered a case of BRD, calves had to demonstrate an absence of abnormal clinical signs attributable to organ systems other than the respiratory system and had to meet the following case definition based on presenting clinical signs: 1) observed clinical signs of BRD evaluated using a visual depression scoring system (Table 2; Perino and Apley, 1998); a minimum depression score of 2 was required for a diagnosis of BRD; and 2) a rectal temperature of >39.8°C (Duff and Galyean, 2007).

Calves with visual clinical signs of BRD and a temperature of <39.8°C were not treated. Animals not treated for BRD on initial evaluation that continued to display clear visual signs of BRD for 2 consecutive days were treated with an antimicrobial regardless of temperature. All calves that met the treatment criteria for BRD were treated with a single subcutaneous (SC) dose of 12.5 mg of enrofloxacin/kg (Baytril, Bayer Animal Health, Shawnee Mission, KS). If the calf met the temperature criteria for a second time 72 h postinitial treatment, the calf was treated with 40 mg/kg of florfenicol SC (Nuflor, Intervet/Schering-Plough Animal Health). If a calf met the treatment criteria for a third time 72 h postsecondary treatment, it received 22 mg/kg oxytetracycline SC (Biomycin 200, Boehringer Ingelheim Vetmedica Inc., St. Joseph, MO). After treatments, cattle were returned to their home pens.

In addition to BRD, other health outcomes that were considered included lameness, scrotal infection, and coccidiosis. A diagnosis of lameness was based on signs of limping and reduced weight bearing on 1 or more limbs during standing and walking. A diagnosis of scrotal infection was based on signs of anorexia, fever, and the presence of swelling and purulent discharge

from the castration site. A diagnosis of coccidiosis was based on signs of diarrhea, anorexia, and the presence of coccidia oocysts on microscopic examination of the feces. Calves with lameness and scrotal infections received 22 mg of oxytetracycline/kg SC (Biomycin 200, Boehringer Ingelheim Vetmedica Inc.), and calves with coccidiosis received 10 mg of amprolium/kg PO (Corid 9.6% oral solution, Merial Ltd.).

The removal of an animal from the study was permitted only for significant illness or injury that compromised the welfare of the animal. All calves that became severely injured or moribund were humanely euthanized. Animals that died or were euthanized during the study were transferred to the Kansas State University Veterinary Diagnostic Laboratory for necropsy and disposal.

Data Collection and Management

All animals were individually weighed on arrival (d 0), before feeding at revaccination on d 14, and at the end of the study on d 28. Time of weighing, scale, and weighing conditions were standardized for all animals at each time point. Feed consumption for each pen was determined on a daily basis by subtracting the weight of feed remaining at the next feeding from the total feed weight assigned to the pen. When animals were removed for health reasons, the amount of feed delivered to the pen and the corresponding animal BW gain in the pen were adjusted accordingly so that calculations for ADG, DMI, and corresponding G:F were based on the number of calves remaining in the pen.

Animal health data recorded for each calf identified as sick included the pull date, the individual animal

Table 2. Depression scoring system used to determine sickness and diagnose bovine respiratory disease (BRD) in calves (Perino and Apley, 1998)

Depression score	Clinical signs
0	Normal, no signs of depression
1	Noticeable depression without apparent signs of weakness. Slower than pen mates but still raises head when approached and does not appear weak; actively follows your movements with a raised head.
2	Marked depression with moderate signs of weakness without a significantly altered gait. Stands with head lowered; will perk up when approached but will return to depressed stance; moves slowly and falls toward back of group, may display signs of weakness such as incoordination.
3	Severe depression with signs of weakness such as a significantly altered gait. Obviously weak; difficulty in moving with group; raises head only when approached closely.
4	Moribund; unable to rise

identification number, body temperature, clinical score, a presumptive diagnosis, BW, and treatment. All data were recorded on data capture sheets that were subsequently compiled, collated in a computer spreadsheet program (Microsoft Office Excel 2007), and verified.

The ancillary production variables [ADG, days on feed (**DOF**), and daily DMI] were calculated for all animals that completed the feeding period. Average daily BW gain and pen-level G:F were calculated using the following equations (Hannon et al., 2009):

$$\text{BW ADG (kg)} = \frac{\text{BW (d 28)} - \text{arrival BW (d 0)}}{\text{DOF}};$$

$$\text{DMI (kg)} = \frac{\text{daily pen feed allocation} - \text{feed remaining at next feeding}}{\text{number of calves in the pen}};$$

$$\text{BW G:F} = \frac{\text{pen level ADG (BW)}}{\text{pen level DMI}}.$$

The frequency of the animal health events (pulls, overall morbidity, BRD morbidity, re-pulls, and BRD relapses) was recorded at pen level and used for statistical analyses (Hannon et al., 2009).

Statistical Analysis

Health, performance, plasma meloxicam, and behavioral data were analyzed using generalized linear mixed models fitted with the GLIMMIX procedure (SAS Inst. Inc., Cary, NC). More specifically, performance outcomes (DMI, ADG, G:F) and meloxicam concentrations were modeled as Gaussian using an identity link function. In turn, the frequency of health events (pull, morbidity, BRD) in a given pen were modeled using a binomial distribution whereby the number of binomial trials was defined by number of animals in a pen. The logit link function was used to model health events,

much as is commonly done with logistic regression. Behavior scores were modeled using a categorical multinomial distribution fitted with a cumulative logit link function, again as is commonly done with polytomous logistic regression. Pen served as the experimental unit for all outcomes. Least squares means estimates for each treatment group and the corresponding estimated SE are reported. Pairwise comparisons were conducted using Bonferroni's method to adjust for multiple comparisons and avoid inflation of type I error rate. Statistical significance for these multiple comparisons was designated a priori as a *P*-value ≤ 0.05 .

For the statistical models on performance outcomes, the linear predictor included the fixed effects of gonadal status (CAST/STR), drug treatment (MEL/CONT), time (d 14 and 28), and all 2- and 3-way interactions. Also included in the model were the random blocking effect of lot and the random effect of pen to recognize the experimental unit for treatment groups. Repeated observations within a pen were modeled using a compound symmetry residual variance-covariance structure. For DMI, the residual variance-covariance was expanded to accommodate heterogeneous variances at each time period. In turn, for meloxicam concentrations measured 24 h after drug administration, the linear predictor included the fixed effect of gonadal status (CAST/STR) and the random blocking factor of lot. For all models fitted on Gaussian responses, Satterthwaite method was used to estimate degrees of freedom and Kenward-Rogers was used for bias correction in SE estimation. Newton-Raphson with ridging was the estimation algorithm implemented. Model assumptions were evaluated using externally studentized residuals and were considered to be appropriately met.

For health events and for behavioral scores at each period of observation, the linear predictor for the statistical model included the fixed effects of gonadal status (CAST/STR), drug treatment (MEL/CONT), and their 2-way interaction. Entry BW did not enhance model fit and thus was excluded from the final model.

Table 3. Study removal and mortality rate in calves receiving either lactose placebo (CONT; 1 mg/kg) or meloxicam (MEL; 1 mg/kg) suspended in water and administered per os, 24 h before processing¹

Item	Experimental group, No. (%)			
	CAST		STR	
	CONT	MEL	CONT	MEL
Number enrolled	74	71	55	58
Completed study	73	67	53	57
Study removal	1 (1%)	4 (6%)	2 (4%)	1 (2%)
Mortality rate	0	0	1 (2%)	0
Reason for removal				
Lameness	1 (1%)	2 (3%)	1 (2%)	1 (2%)
Chronic coccidiosis	0	1 (1%)	0	0
Neurological symptoms	0	1 (1%)	0	0
Pen death	0	0	1 (2%)	0

¹On d 1, bulls were surgically castrated (CAST) and steers were processed without castration (STR).

Table 4. Pen-level mean (\pm SEM) estimates for ADG, DMI, and G:F during 28 d on feed in bulls castrated on arrival (CAST) and steers (STR) receiving either lactose placebo (1 mg/kg) or meloxicam (1 mg/kg) suspended in water and administered per os, 24 h before processing¹

Item	CAST						STR						P-value				
	Placebo		Meloxicam		Placebo		Meloxicam		Placebo		Meloxicam						
	1 to 14 DOF ²	15 to 28 DOF	1 to 14 DOF	15 to 28 DOF	Sex	Sex \times Trt	Sex \times DOF	Trt \times DOF	Sex \times Trt \times DOF								
ADG, kg	0.78 (0.18)	1.54 (0.18)	0.95 (0.18)	1.50 (0.18)	1.72 (0.18)	1.37 (0.18)	1.51 (0.18)	1.46 (0.18)	0.972	0.076	0.302	0.002	0.001	0.302	0.002	0.845	0.313
DMI, kg	4.70 (0.22)	6.95 (0.31)	4.80 (0.22)	7.01 (0.31)	5.26 (0.22)	7.39 (0.31)	5.06 (0.22)	7.23 (0.31)	0.733	<0.001	0.352	0.726	0.016	0.352	0.726	0.981	0.849
G:F	0.16 (0.03)	0.22 (0.03)	0.19 (0.03)	0.21 (0.03)	0.32 (0.03)	0.19 (0.03)	0.30 (0.03)	0.20 (0.03)	0.727	0.065	0.335	<0.001	<0.001	0.335	<0.001	0.949	0.326

¹On d 1, bulls were surgically castrated and steers were processed without castration.

²DOF: days on feed.

³Trt: treatment (meloxicam or placebo).

The random effect of lot was also fit in the linear predictor as a blocking factor to account for variability in health events between lots. In addition, pen nested within gonadal status and drug treatment was incorporated in the linear predictor to recognize pen as the experimental unit for these factors. For binomial responses, inference was conducted after checking for absence of overdispersion based on the Pearson χ^2 /degrees of freedom fit statistic. Model parameters were estimated using Laplace integral approximation to maximum likelihood.

Kaplan-Meier plots for cumulative pull rate, crude morbidity, and BRD morbidity for CAST and STR groups were generated using GraphPad Prism (GraphPad Software, La Jolla, CA). The endpoint of interest was survival time, which was defined as the time to first pull, first treatment, first treatment for BRD, or the end of the study in days. In the data set, the variable group represented the drug treatment category (MEL or CONT), the variable time represented the disease-free survival time, and the variable status was used as a censoring indicator, with the value 1 indicating an event time and the value 0 indicating a censored time. We identified group as strata and tested the null hypothesis that the 2 groups had equal survival curves using the log-rank (Mantel-Cox) test. If the *P*-value for the log-rank test was <0.05, this was evidence to reject the null hypothesis. The slope of the curve was used to compute a hazard ratio and its confidence interval using the Mantel Haenszel approach to compare the rate of an event occurring in the 2 treatments over time.

RESULTS

After randomization, the mean (\pm SD) BW was 248.32 \pm 16.20 kg in the CONT-CAST group, 247.66 \pm 16.90 kg in the MEL-CAST group, 245.04 \pm 15.02 kg in the CONT-STR group, and 244.72 \pm 15.65 kg in the MEL-STR group, respectively. After 28 d, 73 of 74 calves in the CONT-CAST group, 67 of 71 calves in the MEL-CAST group, 53 of 55 calves in the CONT-STR group, and 57 of 58 calves in the MEL-STR group completed the study. One calf in the CONT-STR group died from necrotizing diffuse phlebitis of the external iliac and femoral veins with associated thrombo-embolic pneumonia. Lameness accounted for removal of 1 calf from the CONT-CAST, CONT-STR, and MEL-STR groups, respectively, and 2 calves from the MEL-CAST group (Table 3). One calf was removed from the MEL-CAST group with chronic coccidiosis, and another was removed with neurological symptoms.

Performance

Based on evidence for a sex \times DOF interaction (*P* = 0.0022), ADG of CAST calves was less than those of STR calves only at 14 d, but no evidence (*P* = 0.45) for a difference was apparent at 28 d (Table 4). There was no evidence of an effect of MEL administration (*P*

= 0.972) on ADG. The CAST calves had a 0.65 ± 0.17 kg/d increase in ADG from d 15 to 28 compared with d 1 to 14 ($P = 0.0011$). In contrast, STR calves had a 0.20 ± 0.17 kg/d decrease in ADG over the corresponding period, but this was not significantly different from zero ($P = 0.26$). Furthermore, STR calves had a 0.74 ± 0.14 kg/d greater ADG between d 1 and 14 ($P < 0.001$) compared with CAST calves, but evidence for this difference was not apparent between d 15 and 28 ($P = 0.45$).

Regardless of MEL treatment, pen-level DMI was less in CAST calves than in STR calves ($P = 0.016$; Table 4). In either gonadal group, there was no evidence for an effect of MEL administration ($P = 0.73$) on DMI. However, DMI was greater at d 28 compared with d 14 in both CAST and STR calves ($P < 0.001$) irrespective of treatment.

There was no evidence of an effect of MEL administration ($P = 0.73$) on G:F (Table 4). Regardless of MEL treatment, CAST calves showed no evidence for a difference in G:F from d 15 to 28 compared with d 1 to 14 ($P = 0.16$). In contrast, STR calves had a 0.12 ± 0.03 kg/d decrease in G:F over the corresponding period ($P = 0.0004$). Furthermore, STR calves had a 0.13 ± 0.02 greater G:F between d 1 and 14 ($P < 0.001$) compared with CAST calves but evidence for this difference was not apparent between d 15 and 28 ($P = 0.31$).

Health

The pen-level first pull rate was greater in the CONT-CAST ($45.19 \pm 11.1\%$) compared with the MEL-CAST ($25.83 \pm 9.0\%$) calves ($P = 0.038$; Table 5). Pull rate in STR calves was not significantly different between the 2 drug treatments ($P = 0.78$). However, pull rate was greater in the CONT-CAST calves compared with the CONT-STR calves ($P = 0.007$) but not significantly dif-

ferent between the MEL-CAST and MEL-STR calves ($P = 0.43$). The overall case distribution is presented in Figure 2a and b. Overall morbidity rate was marginally greater in CAST calves than in STR calves regardless of treatment ($P = 0.08$). No evidence for treatment differences on overall morbidity was apparent ($P = 0.28$).

The incidence of BRD was marginally greater in CAST calves than STR calves ($P = 0.06$), but there was no evidence for a difference in overall morbidity attributable to BRD between MEL treatment groups ($P = 0.31$). The incidence of BRD was greater in CONT-CAST compared with MEL-CAST calves ($P = 0.003$) but not significantly different between CONT-STR and MEL-STR calves ($P = 0.67$). Morbidity was greater in the CONT-CAST compared with CONT-STR calves ($P = 0.0006$), but there was no evidence for a difference between the MEL-CAST and MEL-STR calves ($P = 0.68$).

The first re-pull rate was not significantly different between CAST and STR calves ($P = 0.14$) or between drug treatment groups ($P = 0.99$). First BRD retreatment rate was not significantly different between sex ($P = 0.60$) and drug treatment ($P = 0.70$; Table 6). There was also no evidence for a difference between CAST and STR calves ($P = 0.66$) or treatment groups ($P = 0.64$) for calves pulled a third time. Similarly, the third BRD treatment rate did not differ significantly between CAST and STR calves ($P = 0.37$) or between drug treatment ($P = 0.94$).

Log-rank (Mantel-Cox) tests indicated that placebo-treated and MEL-treated calves had dissimilar survival curves for first pull rate, overall morbidity rate, and BRD morbidity rate ($P = 0.004$; Figure 3a and b; Table 7). Furthermore, survival curve comparisons for first pull rate and BRD morbidity rate indicated a greater hazard ratio between MEL-CAST and CONT-CAST calves ($P = 0.016$) and CONT-CAST and CONT-STR

Table 5. Estimated probability of health events (\pm SEM) adjusted for pen in bulls castrated on arrival (CAST) and steers (STR) receiving either lactose placebo (1 mg/kg) or meloxicam (1 mg/kg) suspended in water and administered per os, 24 h before processing¹

Item	Experimental group				<i>P</i> -value		
	CAST		STR		Sex	Trt ²	Sex \times Trt
	Placebo	Meloxicam	Placebo	Meloxicam			
Population at risk	74	71	55	58			
Pulls, %	45.2 ^{a,x} (11.1)	25.8 ^y (9.0)	19.7 ^b (6.0)	17.1 (8.7)	0.01	0.06	0.45
Overall morbidity, %	35.0 ^a (16.5)	21.1 (12.1)	13.3 ^b (8.6)	14.4 (10.8)	0.07	0.28	0.36
Bovine respiratory disease morbidity, %	33.8 ^{a,x} (15.4)	17.2 ^y (10.7)	9.7 ^b (5.8)	12.6 (10.2)	0.06	0.31	0.21

^{a,b}Indicate differences between bulls and steers treated with placebo ($P < 0.05$). No evidence for differences was apparent among calves treated with meloxicam.

^{x,y}Indicate differences in bulls treated with placebo vs. meloxicam ($P < 0.05$). No evidence for differences between placebo and meloxicam was apparent in steers.

¹On d 1, bulls were surgically castrated and steers were processed without castration.

²Trt: treatment (Meloxicam or placebo).

Table 6. Estimated probability of re-treatment health events (\pm SEM) adjusted for pen in bulls castrated on arrival (CAST) and steers (STR) receiving either lactose placebo (1 mg/kg) or meloxicam (1 mg/kg) suspended in water and administered per os, 24 h before processing¹

Item	Experimental group				<i>P</i> -value		
	CAST		STR		Sex	Trt ²	Sex \times Trt
	Placebo	Meloxicam	Placebo	Meloxicam			
First re-pull rate, %	43.7 (14)	52.6 (8)	27.1 (16)	69.9 (21)	0.14	0.99	0.31
First bovine respiratory disease relapse rate, %	33.3 (12)	35.7 (14)	33.3 (22)	50.0 (20)	0.60	0.70	0.70

¹On d 1, bulls were surgically castrated and steers were processed without castration.

²Trt: treatment (meloxicam or placebo). Meloxicam: Unichem Pharmaceuticals USA Inc., Rochelle Park, NJ.

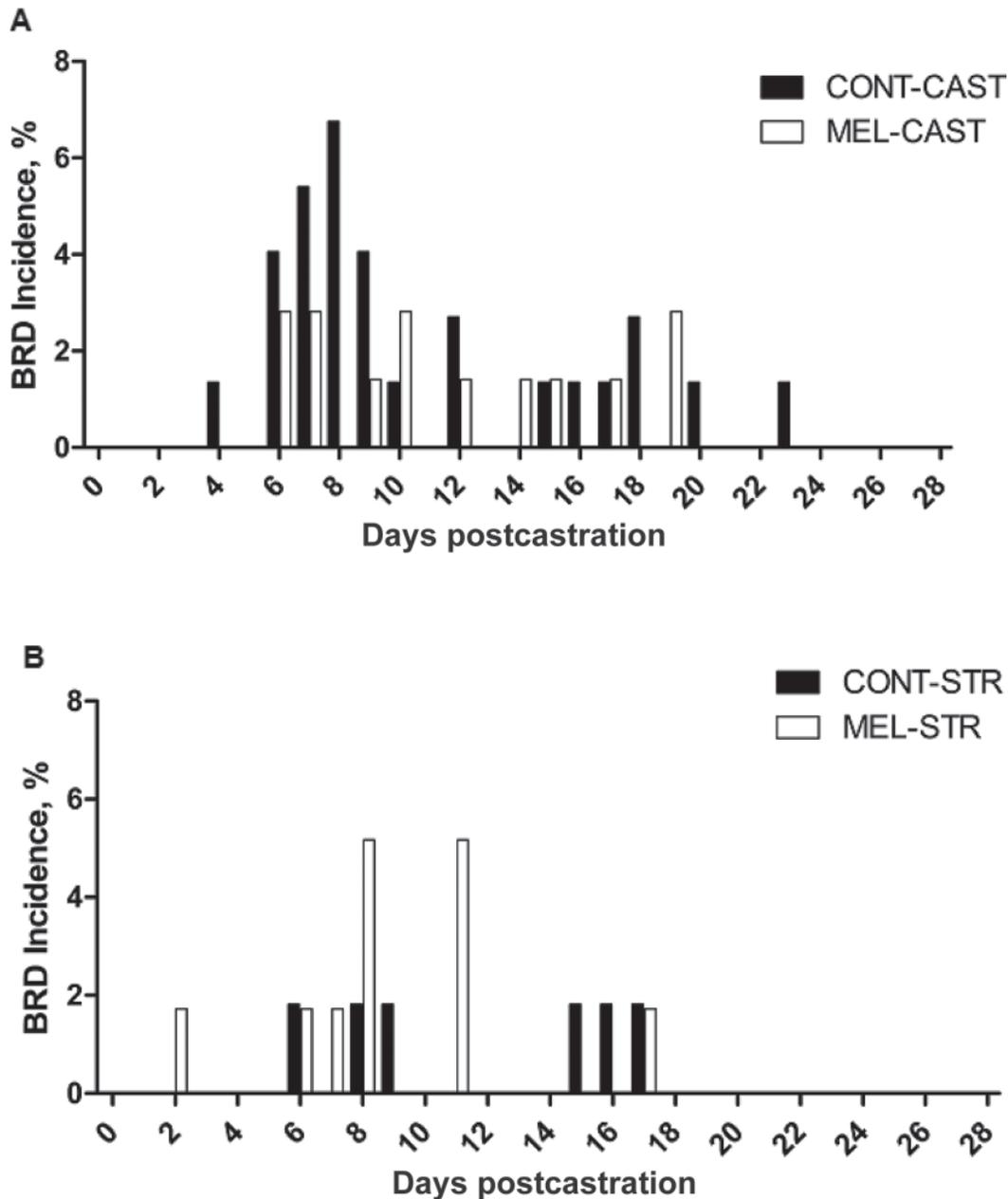


Figure 2. Morbidity distribution pattern in bulls (panel A) and steers (STR; panel B) administered lactose placebo (CONT; 1 mg/kg) or meloxicam (MEL; 1 mg/kg, Unichem Pharmaceuticals USA Inc., Rochelle Park, NJ) suspended in water per os, 24 h before castration (CAST). BRD = bovine respiratory disease.

calves ($P = 0.003$). Other survival curve comparisons for first pull rate and BRD morbidity rate were not significantly different ($P > 0.2$). A hazard ratio that approached statistical significance ($P = 0.073$) was identified for overall morbidity rate between MEL-CAST and CONT-CAST groups, and a hazard ratio occurred between CONT-CAST and CONT-STR groups ($P = 0.003$). Other survival curve comparisons were not significantly different ($P > 0.2$).

Behavior

At the time of dosing with meloxicam (d 0), the relative frequency of temperament score 1 was greater among STR than CAST calves ($P = 0.0019$; Figure 4), thus indicating calmer temperament in the former. This difference between STR and CAST calves was also apparent at castration (d 1), whereby CAST calves showed more frequent escape behaviors recorded than STR calves ($P < 0.001$). However, evidence for these differences was not apparent at revaccination, which is 14 d after castration ($P = 0.22$). Moreover, there was no evidence for differences in behavior between MEL and CONT calves at any of the time points evaluated ($P > 0.35$).

Meloxicam Concentrations

The administered dose of meloxicam rounded down to the nearest whole tablet ranged from 0.89 to 1.00 mg/kg. Sorting and drug administration commenced at around 0800 h and was concluded by 1030 h and therefore lasted approximately 2 min per calf. The mean (\pm SEM) plasma meloxicam concentration at the time of castration, approximately 24 h after treatment, was 6.01 ± 0.07 μ g/mL in CAST and 5.97 ± 0.07 μ g/mL in STR calves ($P = 0.70$; Figure 5). No outward adverse events associated with NSAID administration (e.g., gastrointestinal bleeding, clotting deficits, or anorexia) were noted after PO administration of meloxicam.

DISCUSSION

Castration of male calves destined for beef production is one of the most common livestock management practices performed in the United States, amounting to approximately 7 million procedures per year (USDA NASS, 2011). It is estimated that 41% of beef operations in the United States do not castrate bull calves before sale and approximately 1 of 5 operations (18.4%) do not castrate calves until they are over 122 d old (USDA, 2008). Castration in weaned calves is stressful and affects profitability by reducing performance and increasing susceptibility to disease, especially BRD (Massey et al., 2011). Bovine respiratory disease control in highly stressed cattle is predicated on the administration of vaccines and prophylactic antimicrobials; however, these may be ineffective in preventing disease outbreaks in high-risk cattle (Duff and Galylean,

2007). To our knowledge, this study is the first to test the hypothesis that oral administration of meloxicam, an NSAID with a long plasma elimination half-life, at the time of castration, may improve the health and performance of calves after castration.

A review by Bretschneider (2005) found that castration-associated BW loss reported in the published literature increased quadratically with age. In this review, a mean reduction in DMI of $20.5 \pm 5\%$ was reported in the published reports during the first 2 wk after surgical castration in 5-mo-old calves. Massey et al. (2011)

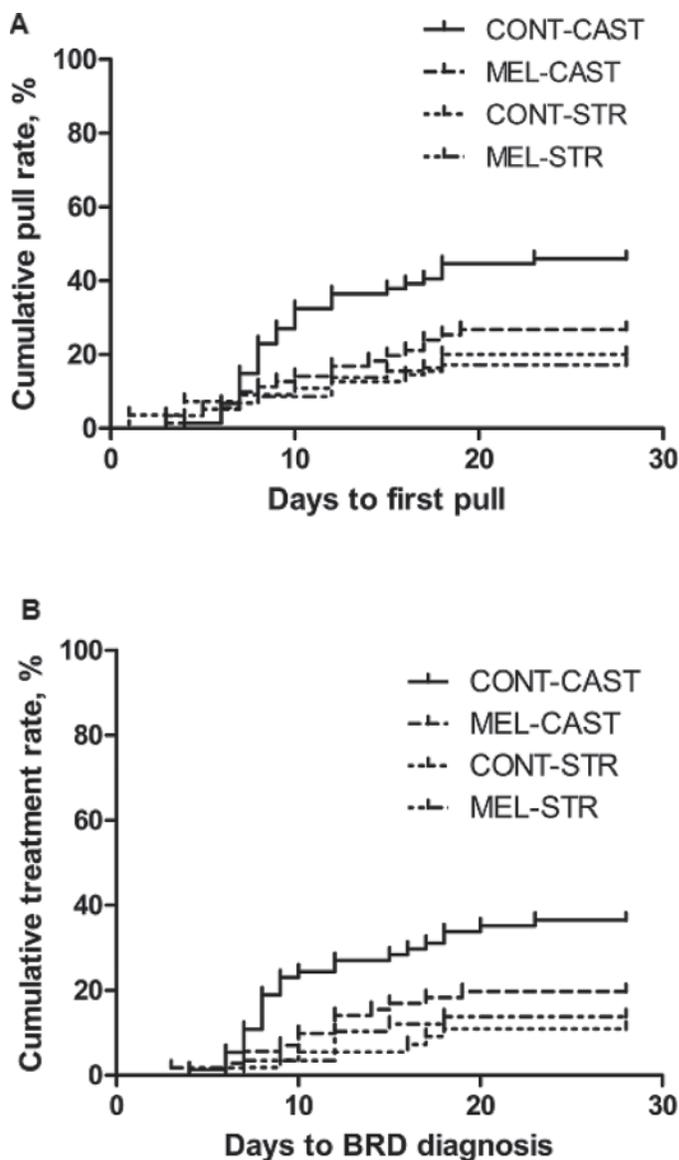


Figure 3. Kaplan-Meier survival curve depicting cumulative pull rate (panel A) and bovine respiratory disease (BRD) treatment rate (panel B) in calves administered lactose placebo (CONT; 1 mg/kg) or meloxicam (MEL; 1 mg/kg, Unichem Pharmaceuticals USA Inc., Rochelle Park, NJ) per os, suspended in water, 24 h before castration. On d 1, bulls were surgically castrated (CAST) and steers were submitted to processing without castration (STR). First pull rate was significantly greater in CONT-CAST calves compared with MEL-CAST calves ($P = 0.016$) and CONT-STR calves ($P = 0.0029$). The BRD morbidity rate was significantly greater in CONT-CAST calves compared with MEL-CAST calves ($P = 0.0230$) and CONT-STR calves ($P = 0.0009$).

Table 7. Log-rank (Mantel-Cox) and Mantel Haenszel hazard ratio comparison between cumulative incidence of first pull, overall morbidity, and bovine respiratory disease (BRD) morbidity in calves receiving either lactose placebo (CONT; 1 mg/kg) or meloxicam (MEL; 1 mg/kg, Unichem Pharmaceuticals USA Inc., Rochelle Park, NJ) suspended in water and administered per os, 24 h before castration¹

Item	Log-rank χ^2	P-value	Survival curve comparison	Hazard ratio	95% CI		P-value
					Lower (HR)	Upper (HR)	
First pull rate	16.73	0.0008	CONT-CAST vs. MEL-CAST	1.97			0.016
			MEL-STR vs. CONT-STR	1.18	0.50	2.79	0.71
			MEL-CAST vs. MEL-STR	1.59	0.76	3.32	0.244
			CONT-CAST vs. CONT-STR	2.48	1.37	4.51	0.0029
Overall morbidity rate	13.26	0.0041	CONT-CAST vs. MEL-CAST	1.73	0.95	3.16	0.073
			MEL-STR vs. CONT-STR	0.83	0.31	2.22	0.71
			MEL-CAST vs. MEL-STR	1.58	0.72	3.43	0.25
			CONT-CAST vs. CONT-STR	2.86	1.44	5.68	0.003
BRD morbidity rate	16.89	0.0007	CONT-CAST vs. MEL-CAST	2.06	1.11	3.82	0.023
			MEL-STR vs. CONT-STR	0.78	0.27	2.23	0.64
			MEL-CAST vs. MEL-STR	1.49	0.64	3.47	0.36
			CONT-CAST vs. CONT-STR	3.23	1.62	6.45	0.0009

¹On d 1, bulls were surgically castrated (CAST) and steers were submitted to simulated castration (STR). CI = confidence interval; HR = hazard ratio.

evaluated records for 2,190 bulls and 1,190 steers and calculated an average ADG of 1.55 kg/d in steers (castrated prearrival) and 1.32 kg/d in bulls (castrated postarrival). The results of the present study report a similar decrease in performance in CAST calves over 14 d after castration. However, from d 14 to 28 there was evidence of compensatory growth in the castrated calves. The timeframe of performance loss suggests that this was likely associated with reduced frequency of feeding and watering bouts in castrated calves rather than testosterone withdrawal (Daniels et al., 2000; Bretschneider, 2005).

Administration of the NSAID ketoprofen before surgical castration increased feeding and rumination activities and reduced pain-associated behaviors in treated calves compared with untreated controls (Ting et al., 2003). Earley and Crowe (2002) demonstrated that calves receiving ketoprofen combined with local anesthesia before surgical castration had a greater ADG during the 35 d after castration compared with untreated calves. However, an increase in DMI or improved G:F was not reported. Baldridge et al. (2011) found that calves receiving 2.5 to 5 mg of sodium salicylate/mL of drinking water beginning 72 h before concurrent surgical castration and dehorning and continuing for 48 h after surgery had a greater ADG during the 13 d after concurrent castration and dehorning than untreated calves. Although these findings support the hypothesis that extended exposure to an NSAID may improve growth and performance after castration, this was not observed after meloxicam administration in the present study. Studies evaluating the effect of meloxicam on individual animal feeding behavior and intakes after castration are needed to fully assess drug effects.

In the present study, calves in the CONT-CAST group were at greater risk of being identified as requiring treatment for disease compared with CONT-STR

calves. Pinchak et al. (2004) reported 60% morbidity in stocker calves (average BW = 216 kg) castrated after arrival compared with 28% morbidity in cohort steers. Berry et al. (2001) reported a 93% pull rate in bulls castrated on arrival compared with a 50% pull rate in calves received as steers. Furthermore, 59% of castrated calves were treated at least once compared with 33% of steers in this study. Of calves castrated on arrival, 23% were retreated. Daniels et al. (2000) found that calves castrated on arrival at a feedlot (BW = 158 ± 14 kg) had a 36% incidence of morbidity compared with 19% morbidity in calves received as steers. This is similar to the morbidity rate reported in the present study in the CONT-CAST calves.

The risk of local or systemic disease after castration is increased by stress and postsurgical immunosuppression (Earley and Crowe, 2002). Surgical castration is associated with increased circulating cortisol and haptoglobin concentrations and decreased gamma-interferon production (Fisher et al., 1997; Earley and Crowe, 2002). An increase in cortisol and haptoglobin causes a suppression of lymphocyte function and a decrease in gamma-interferon is associated with impaired cell-mediated immunity and reduced response to antigens. Earley and Crowe (2002) found that administration of ketoprofen decreased cortisol and haptoglobin concentrations and prevented suppression of the gamma-interferon response. This finding suggests that ketoprofen administration may reduce immunosuppression associated with surgical castration, and it could be hypothesized that other NSAID, such as meloxicam, may have similar effects. This may explain why the incidence of BRD in MEL-CAST was significantly less than in the CONT-CAST group in the present study; however, studies specifically designed to evaluate the effect of meloxicam on immune function after castration are needed to assess this further.

Meloxicam is an NSAID of the oxicam class that is approved in the European Union for adjunctive therapy of acute respiratory disease, diarrhea, and acute mastitis when administered at 0.5 mg/kg intravenously (IV) or SC (EMA, 2009). Although studies reporting health and performance benefits after NSAID administration before castration are deficient in the published literature, meloxicam administration has been associ-

ated with improved ADG in calves treated for clinical BRD (Fritton et al., 2005). Recently, meloxicam was approved in Canada as an aid in improving appetite and BW gains when administered at the onset of diarrhea and for relief of pain after disbudding of horn buds in calves less than 3 mo of age. Heinrich et al. (2009) demonstrated that 0.5 mg of meloxicam/kg intramuscularly combined with a cornual nerve block reduced

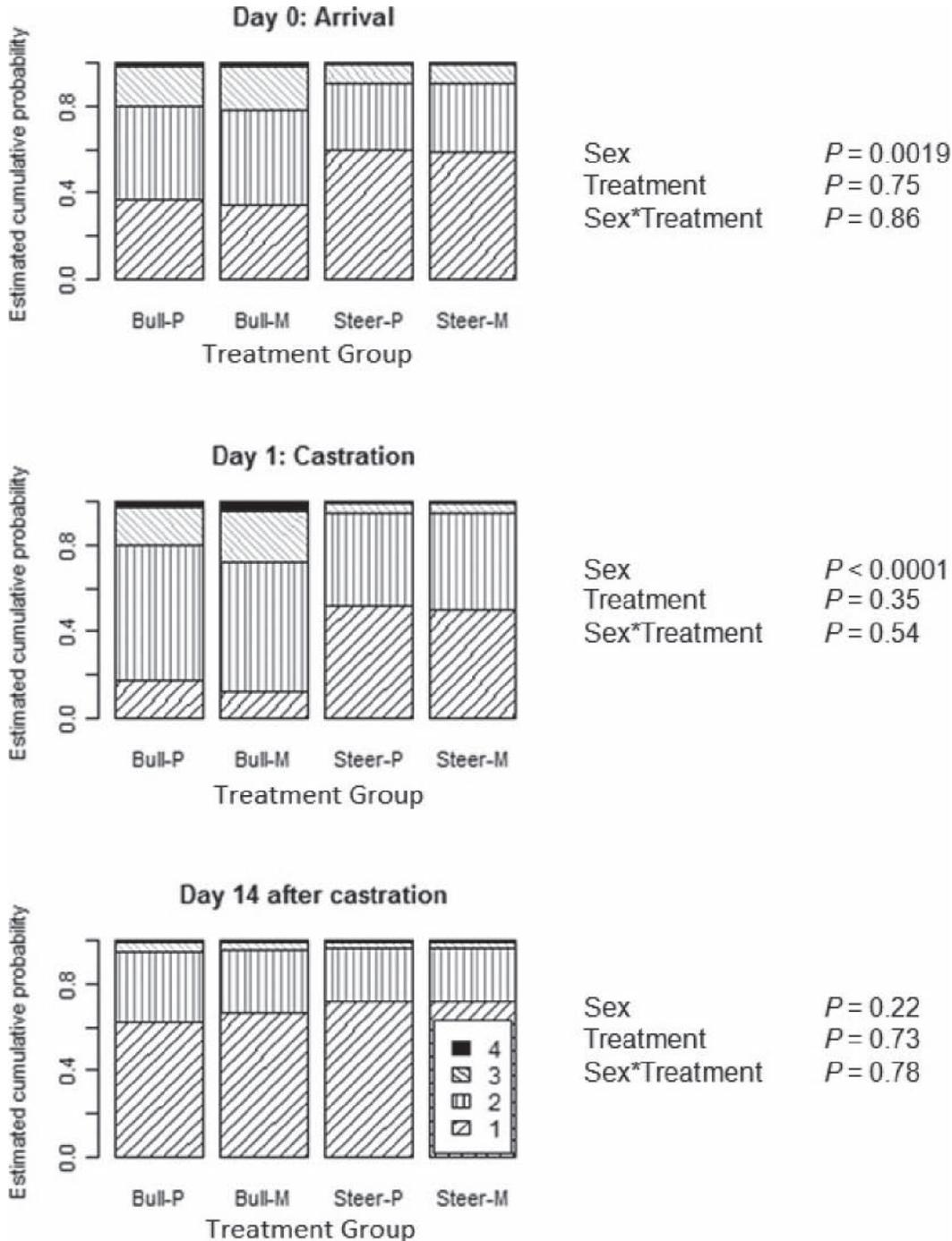


Figure 4. Estimated cumulative probabilities of temperament scores in bulls and steers at arrival (d 0), castration (d 1), and 14 d after castration. Animals were receiving either lactose placebo (P; 1 mg/kg) or meloxicam (M; 1 mg/kg, Unichem Pharmaceuticals USA Inc., Rochelle Park, NJ) suspended in water and administered per os, 24 h before processing with or without castration. Temperament scores are 1 = calm, no movement; 2 = restless shifting; 3 = squirming, occasional shaking of the chute; 4 = continuous vigorous movement and shaking of the chute, rearing, twisting, and struggling.

serum cortisol response longer compared with calves receiving only local anesthesia before cauterizing. This suggests that meloxicam may mitigate pain and distress associated with painful procedures such as castration similar to what has been reported after ketoprofen administration (Earley and Crowe, 2002).

The pharmacokinetics of meloxicam after PO and IV administration have been described recently (Coetzee et al., 2009, 2011). A mean peak plasma concentration of 3.10 $\mu\text{g/mL}$ (range: 2.64 to 3.79 $\mu\text{g/mL}$) was recorded at 11.64 h (range: 10 to 12 h) with a half-life of 27.54 h (range: 19.97 to 43.29 h) after oral meloxicam administration at 1 mg/kg (Coetzee et al., 2009). Based on these data, meloxicam was administered 24 h before castration in the present study to ensure that peak plasma drug concentrations were achieved before the onset of tissue damage. It is noteworthy that the mean plasma meloxicam concentration at the time of castration was greater in the present study than previously reported. This is likely due to the fact that feed was not withheld from calves in the pharmacokinetics study before dosing, which likely delayed drug absorption (Coetzee et al., 2009). Calves in the present study had been shipped over 12 h before treatment and the rumen was likely relatively empty, which probably reduced the amount of drug binding to feed.

Nonsteroidal anti-inflammatory drugs produce analgesia and reduce inflammation by inhibiting the enzyme cyclooxygenase and subsequent PG production in the peripheral tissues and central nervous system (Ochroch et al., 2003). Surgery-induced pain consists of 2 phases: an immediate incisional phase and a prolonged inflammatory phase that arises primarily due to tissue damage (Kissin, 2000; Gottschalk and Smith, 2001). The goal of administering MEL to calves before processing was principally to mitigate pain associated with inflammation after castration because NSAID do not produce effects that would significantly reduce acute, incisional pain. This explains why temperament scores were similar in MEL-treated and placebo-treated CAST calves in this study. In the present report, CAST calves demonstrated behavior causing more shifting and shaking of the chute than STR calves on arrival and during castration. This likely reflects temperament differences between CAST and STR related to prior handling events and also distress associated with the castration procedure.

The connection between meloxicam administration and health benefits observed in bull calves castrated on arrival may be partially supported by the lack of evidence of analogous treatment effect in calves processed as steers. We speculate that this is due to the prolonged anti-inflammatory properties of meloxicam mitigating the negative health effects of inflammation after surgical castration, but further investigation is needed to clarify this association further.

Meloxicam administered to cattle by any route constitutes extra-label drug use because currently no analgesic drugs are specifically approved to provide pain

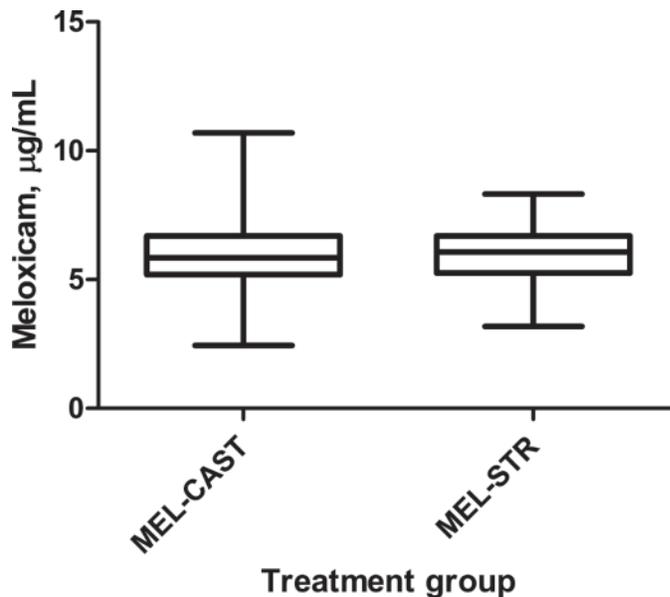


Figure 5. Box and whisker graph showing the median, 25th and 75th percentile, and range of plasma meloxicam (Unichem Pharmaceuticals USA Inc., Rochelle Park, NJ) concentrations at the time of castration in calves administered 1 mg/kg of meloxicam per os in water, 24 h before castration (MEL-CAST), or processing without castration (MEL-STR).

relief in livestock in the United States (Smith et al., 2008). Under the Animal Medicinal Drug Use Clarification Act (**AMDUCA**), extra-label drug use is permitted under veterinary supervision for relief of suffering in cattle provided specific conditions are met (US Food and Drug Administration, 1994). Meloxicam injection (20 mg/mL) is approved for use in cattle in the European Union with a 15-d meat withdrawal and in Canada with a 20-d meat withdrawal time after administration of 0.5 mg/kg IV or SC. Several generic tablet formulations containing meloxicam (7.5 and 15 mg) have been approved for relief of signs and symptoms of osteoarthritis in human medicine. These formulations were used in the present study with a cost of US \$0.30/100 kg of BW. In the absence of FDA-approved analgesic compounds in food animals, use of oral meloxicam tablets for alleviation of pain in cattle can be considered under AMDUCA.

The results of this study suggest that castration reduced pen-level performance from d 1 to 14, but there was no evidence for an effect of NSAID treatment on BW gain or feed intake. Meloxicam administration reduced the pen-level health events in CAST calves, but there was no evidence for meloxicam effects on health events in STR calves. These findings suggest that meloxicam administration before castration in post-weaning calves may decrease the number of castrated calves requiring antimicrobial therapy for pneumonia and lessen the economic impact of BRD in livestock production systems. These results have implications for developing pain mitigation strategies involving NSAID in calves at castration with respect to addressing both animal health and welfare concerns.

LITERATURE CITED

- Baldrige, S. L., J. F. Coetzee, S. S. Dritz, J. B. Reinbold, R. Gehring, J. Havel, and B. Kukanich. 2011. Pharmacokinetics and physiologic effects of intramuscularly administered xylazine hydrochloride-ketamine hydrochloride-butorphanol tartrate alone or in combination with orally administered sodium salicylate on biomarkers of pain in Holstein calves following castration and dehorning. *Am. J. Vet. Res.* 72:1305–1317.
- Berry, B. A., W. T. Choat, D. R. Gill, C. R. Krehbiel, R. A. Smith, and R. L. Ball. 2001. Effect of castration on health and performance of newly received stressed feedlot calves. OSU Animal Science Research Report. Accessed Feb. 23, 2011. <http://www.ansi.okstate.edu/research/research-reports-1/2001/2001%20Berry%20Research%20Report.pdf>.
- Booker, C. W., S. M. Abutarbush, O. C. Schunicht, C. M. Pollock, T. Perrett, B. K. Wildman, S. J. Hannon, T. J. Pittman, C. W. Jones, G. J. Jim, and P. S. Morley. 2009. Effect of castration timing, technique and pain management on health and performance of young feedlot bulls in Alberta. *Bov. Pract.* 43:1–11.
- Bretschneider, G. 2005. Effects of age and method of castration on performance and stress response of beef male cattle. A review. *Livest. Prod. Sci.* 97:89–100.
- Coetzee, J. F., B. Kukanich, R. Mosher, and P. S. Allen. 2009. Pharmacokinetics of intravenous and oral meloxicam in ruminant calves. *Vet. Ther.* 10:E1–E8.
- Coetzee, J. F., R. A. Mosher, L. E. Kohake, C. A. Cull, L. L. Kelly, S. L. Mueting, and B. Kukanich. 2011. Pharmacokinetics of oral gabapentin alone or co-administered with meloxicam in ruminant beef calves. *Vet J.* 190:98–102.
- Coetzee, J. F., A. Nutsch, L. A. Barbur, and R. M. Bradburn. 2010. A survey of castration methods and associated livestock management practices performed by bovine veterinarians in the United States. *BMC Vet. Res.* 6:12.
- Daniels, T. K., J. G. P. Bowman, B. F. Sowell, M. E. Branine, and M. E. Hubbert. 2000. Effects of metaphylactic antibiotics on behavior of feedlot calves. *Prof. Anim. Sci.* 16:247–253.
- Duff, G. C., and M. L. Galyean. 2007. BOARD-INVITED REVIEW: Recent advances in management of highly stressed, newly received feedlot cattle. *J. Anim. Sci.* 85:823–840.
- Earley, B., and M. A. Crowe. 2002. Effects of ketoprofen alone or in combination with local anesthesia during the castration of bull calves on plasma cortisol, immunological, and inflammatory responses. *J. Anim. Sci.* 80:1044–1052.
- European Agency for the Evaluation of Medicinal Products (EMA). 2009. Committee for Veterinary Medicinal Products. Meloxicam. Maximum Residue Limit (MRL) Summary Report (2). Accessed Feb. 25, 2011. <http://www.emea.europa.eu/pdfs/vet/mrls/057199en.pdf>.
- Fisher, A. D., M. A. Crowe, E. M. O’Nuallain, M. L. Monaghan, D. J. Prendiville, P. O’Kiely, and M. J. Enright. 1997. Effects of cortisol on in vitro interferon- γ production, acute-phase proteins, growth, and feed intake in a calf castration model. *J. Anim. Sci.* 75:1041–1047.
- Friton, G. M., C. Cajal, and R. Ramirez-Romero. 2005. Long-term effects of meloxicam in the treatment of respiratory disease in fattening cattle. *Vet. Rec.* 156:809–811.
- Gottschalk, A., and D. S. Smith. 2001. New concepts in acute pain therapy: Preemptive analgesia. *Am. Fam. Physician* 63:1979–1984.
- Hannon, S., T. Perrett, B. Wildman, O. Schunicht, A. Vogstad, R. K. Fenton, L. Borciaga-Robles, C. Pollock, G. K. Jim, J. Berg, and C. Booker. 2009. Efficacy of a florfenicol-flunixin meglumine combination product versus tulathromycin or ceftiofur crystalline free acid for the treatment of undifferentiated fever in feedlot calves. *Vet. Ther.* 10:E1–E18.
- Heinrich, A., T. F. Duffield, K. D. Lissemore, E. J. Squires, and S. T. Millman. 2009. The impact of meloxicam on postsurgical stress associated with cautery dehorning. *J. Dairy Sci.* 92:540–547.
- Kissin, I. 2000. Preemptive analgesia. *Anesthesiology* 93:1138–1143.
- Massey, C., K. C. Dhuyvetter, R. V. Llewelyn, and D. A. Blasi. 2011. Castration and morbidity and their effects on performance, carcass quality, and price differentials for bulls and steers. *Prof. Anim. Sci.* 27:19–28.
- Ochroch, E. A., I. A. Mardini, and A. Gottschalk. 2003. What is the role of NSAIDs in pre-emptive analgesia. *Drugs* 63:2709–2723.
- Perino, L. J., and M. D. Apley. 1998. Clinical trial design in feedlots. Pages 343–365 in *Veterinary Clinics of North America: Food Animal Practice*. E. Hunt and G. L. Stokka, ed. W. B. Saunders Co., Philadelphia, PA. Vol. 14. No. 2.
- Pinchak, W. E., D. R. Tolleson, M. McCloy, L. J. Hunt, R. J. Gill, R. J. Ansley, and S. J. Bevers. 2004. Morbidity effects on productivity and profitability of stocker cattle grazing in the Southern Plains. *J. Anim. Sci.* 82:2773–2779.
- Smith, G. W., J. L. Davis, L. A. Tell, A. I. Webb, and J. E. Riviere. 2008. Extralabel use of nonsteroidal anti-inflammatory drugs in cattle. *J. Am. Vet. Med. Assoc.* 232:697–701.
- Ting, S. T. L., B. Earley, and M. A. Crowe. 2003. Effect of repeated ketoprofen administration during surgical castration of bulls on cortisol, immunological function, feed intake, growth, and behavior. *J. Anim. Sci.* 81:1253–1264.
- USDA. 2008. Beef 2007–08, Part 1: Reference of beef cow-calf management practices in the United States, 2007–2008. #N512–100837–40. USDA-APHIS-VS, CEAH, Fort Collins, CO.
- USDA NASS. 2011. United States Department of Agriculture National Agricultural Statistics Service, Kansas Field Office, Livestock. Kansas Cattle on Feed. Accessed Feb. 25, 2011. http://www.nass.usda.gov/Statistics_by_State/Kansas/Publications/Livestock/Lvstk/2011/livjan.pdf.
- US Food and Drug Administration. 1994. Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA). Accessed Feb. 25, 2011. <http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticAct/FDCAAct/SignificantAmendmentstotheFDCAAct/AnimalMedicinalDrugUseClarification-ActAMDUCAof1994/default.htm>.
- Voisinet, B. D., T. Grandin, J. D. Tatum, S. F. O’Connor, and J. J. Struthers. 1997. Feedlot cattle with calm temperaments have higher average daily gains than cattle with excitable temperaments. *J. Anim. Sci.* 75:892–896.
- Weary, D. M., and D. Fraser. 2004. Rethinking painful management practices. Pages 325–338 in *The Well-Being of Farm Animals: Challenges and Solutions*. 1st ed. G. J. Benson and B. E. Rollin, ed. Blackwell Publishing, Ames, IA.