THESIS

ORAL MELOXICAM AS AN ANCILLARY THERAPY FOR RESPIRATORY DISEASE IN DAIRY CALVES AND USING CASE-BASED TEACHING METHODS IN AN ANIMAL SCIENCE COURSE

Submitted by

Logan Ferree

Department of Animal Sciences

In partial fulfillment of the requirements

For the Degree of Master of Science

Colorado State University

Fort Collins, Colorado

Fall 2022

Master's Committee:

Advisor: Catie Cramer

Tanya Applegate
Lily Edwards-Callaway
Noa Roman-Muniz

ABSTRACT

ORAL MELOXICAM AS AN ANCILLARY THERAPY FOR RESPIRATORY DISEASE IN DAIRY CALVES AND USING CASE-BASED TEACHING METHODS IN AN ANIMAL SCIENCE COURSE

This thesis consists of two projects: assessing the effects of a single dose of oral Meloxicam as an ancillary therapy at time of respiratory disease identification on health and performance in preweaned dairy calves (Project 1) and assessing the effect of case-based teaching compared with lecture-based teaching on students' knowledge and perceptions in a senior undergraduate dairy cattle management course (Project 2).

The objectives of Project 1 were to assess the effects of a single dose of oral meloxicam as an ancillary therapy to an antibiotic (tulathromycin; Draxxin) at time of respiratory disease identification on performance and growth in preweaned dairy calves. A few non-steroidal anti-inflammatory drugs (NSAIDs) have been studied as an ancillary therapy to antibiotics for respiratory disease in preweaned calves (Bednarek et al., 2003; Guzel et al., 2010; Lockwood et al., 2003; Mahendran et al., 2017). However, respiratory disease continues to be one of the leading causes of morbidity and mortality in preweaned dairy calves (USDA, 2018). A recent survey of veterinarians suggests that a single dose of an antimicrobial is not always effective at resolving a case of respiratory disease and warrants further investigation of respiratory disease treatment (Mijares et al., unpublished). To our knowledge, oral meloxicam has not yet been studied as an ancillary therapy to an antibiotic for respiratory disease in preweaned dairy calves.

Oral meloxicam is an NSAID with analgesic and anti-pyretic properties, as well as a low-cost of $0.30/100 kg (Coetzee et al., 2009; McGill and Sacco, 2020). In Project 1, dairy calves on a commercial farm were observed from 0-56 days of age for signs of respiratory disease using the Wisconsin Calf Health Scoring System (McGuirk and Peek, 2014) and lung ultrasound (Ollivett and Buczinski, 2016). Upon identification of respiratory disease, calves were randomly assigned using a predetermined Excel sheet to receive a one-time dose of a placebo (PLA) or meloxicam (MEL) in addition to an antibiotic (tulathromycin; Draxxin) according to the farm's protocol. Following treatment, calves received twice weekly health exams up to 56 days of age (WEAN) that included the Wisconsin Calf Health Score (McGuirk and Peek, 2014), a lung ultrasound score (Ollivett and Buczinski, 2016), and a heart girth measurement (Davis et al., 1961). The heart girth measurement was used to estimate the calf's average daily gain (ADG) from time of respiratory disease identification to the time of weaning (WEAN). The following binary variables were evaluated at the health exam immediately following identification (NEXT) and 7 days following identification (WEEK): attitude, fever, clinical respiratory score (CRS), and lung ultrasound score. The variable respiratory disease status (YES/NO) was evaluated at WEAN. All statistical analyses were performed in SAS v. 9.4 (SAS Institute Inc., Cary, NC). Average daily gain was calculated using a simple linear regression (PROC REG) using the calf's age and the heart girth measurement at each health exam (Davis et al., 1961). A mixed linear model (PROC MIXED) was used to test the hypothesis that calves in MEL would have a higher ADG than calves in PLA and included an LSMEANS statement to produce the estimates ± SEM for ADG by NSAID group. Four separate logistic regressions (PROC GLIMMIX) were used to evaluate the effect of NSAID group on the outcomes attitude, fever, CRS, and lung ultrasound score at NEXT and WEEK, as well as respiratory disease status at WEAN. We did not observe an effect of NSAID group on any of the outcomes at NEXT (P > 0.05), WEEK (P > 0.05), WEAN (P > 0.05), or ADG (P > 0.05). Though we did not observe an effect of NSAID group, Project 1 was the first study of its kind to investigate the effects or oral meloxicam as an ancillary therapy to antibiotics for respiratory disease in preweaned calves in a commercial setting. Further research should be conducted to evaluate the efficacy of oral meloxicam in various commercial settings to account for differing management practices.

The objectives of Project 2 were to determine the effects of case-based (CB) and lecture-based (LB) teaching methods on student performance and to assess students' attitudes toward CB and LB teaching methods in a senior dairy cattle management course. Animal science students need to apply the knowledge acquired during their degree program to real-life scenarios in future careers. Little to no research exists evaluating the effects of case-based (CB; material presented as a case study) and lecture-based (LB; material presented as a lecture) teaching in animal science in higher education. A cross-over study design was conducted over two course modules (1 = "calf health" and 2 = "lameness") with a washout period of 2 wk. Students (n = 25) were randomly assigned to CB or to LB in module 1 and received the other method in module 2. Students completed a pre- and post-quiz in each module that consisted of 10 multiple-choice questions and 3 short-answer questions. Three separate linear mixed regression models were used to assess the effect of teaching method (CB or LB; predictor) on three different continuous outcomes for student performance: change (post-score − pre-score) in short-answer quiz scores, change in multiple-choice quiz scores, and the change in total quiz scores. Students completed an attitude assessment after each module that consisted of 8 Likert-scale statements and 2 free-response questions. Data were deidentified, and two researchers blinded to students' CB or LB status analyzed free responses to identify themes. A logistic regression, which controlled for

module and included student as a repeated measure, was used to determine if the proportion of students who agreed (outcome: yes/no) with each Likert-scale statement was different between CB and LB. There was a tendency for CB teaching methods to improve change in multiple-choice quiz scores ($P = 0.06$). The change in total quiz scores and the change in short-answer quiz scores did not differ between CB and LB groups ($P > 0.1$). For the survey statements "I enjoyed the teaching method used in this module" and "I wish this teaching method was utilized in more of my classes," more students in LB agreed than in CB ($P < 0.05$). The themes preference, perceived benefits, and perceived drawbacks were mentioned in 80%, 44%, and 28% of CB comments, and in 84%, 40%, and 18% of LB comments, respectively, and suggest that students enjoy case studies but prefer to receive information via lecture first.

ACKNOWLEDGEMENTS

I would like to thank my advisor, Dr. Catie Cramer for your never-ending support and guidance over the last two years. Navigating graduate school in the middle of a pandemic was not the most ideal situation and I am grateful for your hands-on involvement and dedication to mentoring me in every way. I always appreciate your positive attitude and have learned so much about how to care for students from watching you, as well as how to perform very efficient health exams on dairy calves! I would like to thank my committee members: Dr. Lily Edwards-Callaway, Dr. Noa Roman-Muniz, and Dr. Tanya Applegate for being willing to serve on my committee and for each providing a unique set of skills and knowledge that made this thesis possible. Thank you to the dairy farms that so graciously allowed us to utilize their facilities to perform research and to every dairy calf that allowed us to ultrasound their lungs, measure their heart girth, collect a blood sample, and pose for photos with them. Thank you to every student that sat through my lectures and took the time to fill out our surveys. I am so grateful for every single volunteer and fellow graduate student that gave their time and talents in the collective effort of data collection! I would like to personally thank my fellow researcher and friend, Grace Larsen, for the tremendous amount of time, effort, and care she dedicated to working alongside me throughout both of my projects. It was an honor to get to watch you grow into an incredible scientist and I am so proud of you! I will forever cherish the relationships and memories that were made during the last two years.

I want to thank my husband, Dan, for being willing to move over 1,000 miles from home to be with me as I attended graduate school. You have supported me every single day along the

way and put up with so many 3:30 am alarms and coverall buckles clanking in the dryer as I was rummaging through the room with my flashlight. Thank you dear for taking this adventure on with me! I couldn't have done it without you. Thank you to my best friend back home, Julie, for answering all of my phone calls and acting just as excited about a new photo of a calf nose as the last! I am so lucky to have your support. Another huge thank you to my best friend in Fort Collins, Tyler, for all the cups of coffee we have shared and the endless encouragement you have so diligently provided and for so confidently believing in me when I didn't! Thank you so much to all my family members for your support and for making sure I was taking care of myself. Thank you all for keeping me company on the phone at some point while I was making a run to ARDEC or organizing lab supplies and for encouraging me to chase my dreams!

DEDICATION

To every dairy calf that allowed me to ultrasound their lungs or take their blood and to every dairy calf there ever will be – thank you. May you be happy and healthy.

TABLE OF CONTENTS

CHAPTER 1: INTRODUCTION

1.0 Introduction

Respiratory disease is responsible for nearly a quarter of preweaned dairy heifer deaths according to producer reported data from 104 operations consisting of approximately 2,500 calves (Taylor et al., 2010; USDA, 2018). Respiratory disease is a multifactorial disease caused by the complex interaction between stressors, pathogens, and the host's immune response that can affect both the upper and lower airways (McGill and Sacco, 2020; Poulsen and McGuirk, 2009). During the preweaning period, dairy calves may experience stressors such as diarrhea, nutritional stress, heat or cold stress, and poor ventilation that alter their immune system (Caswell, 2013; Lago et al., 2006; McGuirk, 2008; Taylor et al., 2010). The industry is constantly gaining new information regarding best practices of calf care (e.g., amount of milk to feed, type of housing) and striving to minimize stressors and prevent disease. When a calf undergoes stress, its immune defenses, such as mucocilliary clearance, are altered and normal commensal pathogens can replicate in the upper respiratory tract (Ackermann et al., 2010; Caswell, 2013). The immune system responds to pathogen replication by initiating an immune response comprised of physiological (e.g., mucocilliary action and inflammation, including fever) and behavioral (e.g., lethargy) components (Hart et al., 1988; Dantzer, 2004; Toaff-Rosenstein et al., 2016). If pathogens overwhelm the innate immune system, the pathogens can invade the lower airway, leading to inflammation in the lungs, or pneumonia (Caswell, 2013; Timsit et al., 2013). Clinical signs of respiratory disease are the manifestation of this immune response and may include nasal or ocular discharge, cough, fever, abnormal breathing, or abnormal lung sounds upon auscultation (McGuirk and Peek, 2014).

The need for accurate detection methods that can differentiate between upper and lower respiratory disease has been noted (Ollivett and Buczinski, 2016). Respiratory disease can be identified using scoring systems that evaluate clinical signs of respiratory disease such as the Wisconsin Calf Health Scoring System (CRS; McGuirk and Peek, 2014; e.g., nasal discharge, ocular discharge, lowered ear position, cough, and fever) and the University of California Davis Bovine Respiratory Disease Scoring System (Love et al., 2014; nasal discharge, ocular discharge, lowered ear position, breathing, cough, and fever). Additionally, lung ultrasound can be used to identify lower respiratory tract disease by detecting the presence of abnormal lung tissue, or pneumonia; the amount of abnormal lung tissue can be quantified through a scoring system (Ollivett and Buczinski, 2016). The CRS and lung ultrasound tools are explained in more detail in subsequent sections; however, these tools can be used to classify respiratory disease based on both the clinical status and lung health of the calf. Cramer et al. (2019) and Ollivett and Buczinski (2016) classified respiratory disease into three categories: upper respiratory tract infection (URT), subclinical pneumonia (SCP), and clinical pneumonia (CP) based on clinical and ultrasound findings. The three categories are defined by Ollivett and Buczinski (2016) as follows: URT = a calf is CRS+ and has a normal ultrasound score; SCP = a calf is CRS- and has an abnormal ultrasound score $\geq$2; CP = a calf is CRS+ and has an abnormal ultrasound score.

Regardless of the type of respiratory disease that a calf is identified with, the recommendation for treatment of respiratory disease is a systemic antimicrobial (Apley, 2009; Francoz et al., 2012). Producers reported treating 16.4% of their calves with an antibiotic for respiratory disease (USDA, 2011) and of the calves identified with respiratory disease, 94.8%

were treated with an antimicrobial (USDA, 2018). Furthermore, a 2005 study in Pennsylvania attributed pneumonia cases to a quarter of all antibiotic usage in preweaned calves (Sawant et al., 2005).

Despite treatment with antibiotics, mortality due to respiratory disease has remained relatively unchanged over the last 20 years, accounting for 21.3-24% of preweaned dairy heifer deaths (USDA, 1994; USDA 2002; USDA, 2007; USDA, 2018). Respiratory disease case fatalities have been reported to range from 0-10.26% (Dubrovsky et al., 2019b; Sivula et al., 1996; Urie et al., 2018) suggesting that current management practices are not always effective at resolving a case of respiratory disease. Because mortality due to respiratory disease has remained relatively the same over time in preweaned dairy heifers, additional and effective disease management practices are needed such as timely detection and treatments of respiratory disease. Researchers have investigated a few non-steroidal anti-inflammatory drugs (NSAIDs; e.g. carprofen, diclofenac sodium, flunixin meglumine, ketoprofen, and meloxicam) as an ancillary therapy to an antibiotic in cattle for the treatment of respiratory disease (Bednarek et al., 2003; Elitok and Elitok, 2004; Guzel et al., 2010; Lockwood et al., 2003). These studies all found that the addition of an NSAID to an antibiotic was associated with improvement in clinical signs of respiratory disease, specifically pyrexia or respiratory rate, in the first 6-48 hours following treatment compared to treatment with an antibiotic alone (Bednarek et al., 2003; Elitok and Elitok, 2004; Guzel et al., 2010; Lockwood et al., 2003). However, respiratory disease continues to be a leading cause of morbidity and mortality therefore continued investigation of treatment methods is warranted.. The use of NSAIDs as therapy in calves with respiratory disease is not yet established or approved in the United States, except under the Animal Medicinal Drug Use Clarification Act (AMDUCA, 1994). The objectives of this literature review are 1) to provide background on morbidity, mortality, and impacts associated with respiratory disease in preweaned dairy calves and 2) synthesize previous literature on the detection and treatment of respiratory disease, with an emphasis on NSAIDs as an ancillary therapy to antibiotics for respiratory disease.

1.1 Impacts of respiratory disease

Respiratory disease is one of the leading causes of morbidity and mortality in preweaned dairy heifers (USDA, 2018). According to producer-reported data collected by the National Animal Health Monitoring System (NAHMS) that included 104 dairy operations and approximately 2,500 calves, concluded 11.2% of preweaned heifers in the U.S. are affected by respiratory disease and 24% of all preweaned heifer deaths are due to respiratory disease (USDA, 2018).

Morbidity

Morbidity due to respiratory disease in preweaned dairy heifers has remained relatively unchanged over the last 20 years, as evidenced by producer-reported data, with 9.0%, 12.4%, and 12.0% dairy heifers affected in 2002, 2007 and 2014 respectively (USDA, 2002; USDA, 2007; USDA, 2018). Within the United States, respiratory disease prevalence ranges from 4-28%, second only to gastrointestinal disease in dairy calves (Dubrovsky et al., 2019a; Karle et al., 2019; Urie et al., 2018). However, it is possible morbidity is underreported as producer-identified respiratory disease lacks sensitivity (Sivula et al., 1996).

Medrano-Galazra et al. (2018) collected clinical and feeding behavior from automatic calf milk feeders across 17 dairy farms and determined the overall calf-level prevalence (defined as number of calves with BRD/total number of calves) of BRD in this Ontario study was 17%

with an observed within-pen prevalence (defined as number of calves with BRD in a pen/total number of calves in a pen) range of 0-28% (Medrano-Galazra et al., 2018). Furthermore, lung ultrasound has been used as a subclinical disease detection tool and is reported to be a sensitive method (Ollivett and Buczinski, 2016). A study reported 59.66% of calves with an abnormal ultrasound score and negative clinical respiratory score at the first respiratory event in the study, supporting potentially underreported incidences of respiratory disease in studies not utilizing a subclinical detection method, such as ultrasound (Cramer and Ollivett, 2019). The variation in detection methods used across studies explains the observed ranges in disease prevalence as some studies utilize only producer reported data, others only utilize a clinical detection method and some utilize both clinical and subclinical detection methods.

Mortality

Respiratory disease not only negatively impacts a calf's ability to thrive but can lead to death. Studies have attributed 19-30% of all calf deaths to respiratory disease (Dubrovsky et al., 2019b; Gulliksen et al., 2009; Sivula et al., 1996). Additionally, Mahendran et al. (2017) reported an increased chance of earlier death in calves with clinical signs of respiratory disease (e.g., pyrexia, cough, or nasal discharge) compared to calves without clinical signs of disease. Likewise, a case of respiratory disease increases a calf's risk of death in the first year of life (Gullisken et al., 2009) as evidence by hazard ratios of 5.6-7.4 (Gulliksen et al., 2009). The reported ranges of mortality due to respiratory disease vary between studies and can be explained by differences in timeliness of detection and intervention, detection methods, treatment protocols, and the definition of respiratory disease used. However, regardless of study and treatment methods, respiratory disease continues to account for a large portion of deaths in preweaned dairy calves (Dubrovsky et al., 2019b; Gulliksen et al., 2009; Sivula et al., 1996; USDA, 2018).

Average daily gain during the preweaning period

Respiratory disease not only impacts a calf by increasing their chance of death, but also affect a calf's growth during and beyond the preweaning period (Cramer and Ollivett, 2019; Cuevas-Gómez et al., 2021; Curtis et al., 2018; Stanton et al., 2012; Virtala et al., 1996). Even when treated with an antibiotic, and in some cases an NSAID, calves that are identified with respiratory disease during the preweaning period gain 0.07 – 0.85 kg/d less than calves that were not affected (Cramer and Ollivett, 2019; Cuevas-Gómez et al., 2021; Curtis et al., 2018; Stanton et al., 2012; Virtala et al., 1996). Furthermore, preweaned calves that experienced a case of respiratory disease gained 10.6 – 16.0 kg/d less in the first 12-14 months of life than calves that did not experience a case (Donovan et al., 1998; Stanton et al., 2012). An important indicator of calf health is weight gain as suggested by Heins et al. (2014) that noted every 1 kg increase in a calf's weight at their first treatment was associated with a 7% reduction in the likelihood of requiring a third treatment for respiratory disease.

Cost of respiratory disease

Respiratory disease not only affects the calf, but also the producer as it is one of the costliest diseases in the dairy industry (Delabouglise et al., 2017). The cost of treating respiratory disease in calves has been estimated at $42.15 per calf, including pharmaceuticals (antibiotics with or without NSAIDs), labor, and repeated treatments, but does not account for long-term losses associated with respiratory disease, such as decreased milk production during first lactation (Dubrovsky et al., 2020; Dunn et al., 2018).

Worker morale

In addition to economic impacts, respiratory disease can affect dairy caretakers' health and well-being (Kolstrup and Hultgren, 2010). Kolstrup and Hultgren (2010) identified an association between employees exhibiting psychosocial symptoms and disease incidence rate, meaning employees that work in a herd with higher disease incidence rates experience more negative emotional experiences than employees in herds with lower disease incidence rates. Dairy caretakers become emotionally invested in the animals they care for and the well-being of the animals greatly impacts their personal well-being. In addition to a relationship between disease and worker morale, a relationship between healthy animals and worker motivation and satisfaction exists (Kolstrup and Hultgren, 2011). The results of Kolstrup and Hultgren (2011) emphasize a correlation between cattle health and dairy worker health, providing further motivation to limit disease on farm and revealing that dairy workers want to provide adequate care to the animals. By providing adequate care, improvements in animal health may be achieved and can result in improved employee satisfaction and wellbeing.

Long term productivity

There is conflicting evidence on a calf's chance of survival to and milk production at first lactation after experiencing respiratory disease in the preweaning period. Respiratory disease has been associated with long term losses as affected calves have lower odds of surviving through their first lactation (Bach, 2011; Rossini, 2004; Schaffer et al., 2016) and produce 525 kg less milk at their first lactation (Dunn et al., 2018) compared to unaffected calves. In comparison, no association between respiratory disease in the pre- and post-weaning period and the odds of surviving to first lactation (Stanton et al., 2012; Teixeira et al., 2017; Dunn et al., 2018), milk production in the first lactation (Svensson and Hultgren, 2008; Stanton et al., 2012; Teixeira et al., 2017), or daily milk production (Closs and Dechow, 2017) have also been reported. The reported differences in milk production could be due to differences in antibiotics used in the studies during, severity of disease, sample size, definition of respiratory disease and detection methods (Closs and Dechow, 2017; Dunn et al., 2018; Svensson and Hultgren, 2008; Stanton et al., 2012; Teixeira et al., 2017). For example, animals in Dunn et al. (2018) were all kept in the herd until the end of their first lactation whereas animals in Teixeira et al. (2017) may have been culled prior to the end of their first lactation and the full effects of lung consolidation on first lactation milk production were not able to be observed. Additionally, Teixeira et al. (2017) performed only one lung ultrasound at time of weaning compared to Dunn et al. (2018) that performed multiple lung ultrasounds throughout the preweaning period, so calves with lung consolidation prior to weaning were not noted in Teixeira et al. (2017), therefore limiting the ability to detect an effect on milk production. Stanton et al. (2012) reported no effect of respiratory disease identified by farm staff in the 60 days following movement to group housing on 305-day milk production at first lactation. The difference in timepoints when respiratory disease status was assessed as well as detection method, could contribute to the difference in reported effects on milk production as the studies methods are not directly comparable.

1.2 Detection

Early detection of respiratory disease can be key to a calf's survival and recovery (McGuirk, 2008). Evaluating calves for clinical and subclinical respiratory disease can quickly be done using clinical scoring systems and lung ultrasound. The Wisconsin Calf Health Scoring system evaluates ear position, ocular discharge, nasal discharge, cough, and rectal temperature on a scale of 0 (normal) to 3 (severely abnormal) to assign calves a clinical respiratory score (CRS; McGuirk and Peek, 2014). A calf is considered positive for respiratory disease if it receives a score ≥2 in at least 2 or more of the clinical respiratory score categories (CRS+; McGuirk and Peek, 2014). The University of California Davis Bovine Respiratory Disease Scoring System evaluates cough, ocular discharge, nasal discharge, fever, abnormal respiration, and head tilt or ear droop and assigns a specific score of 2, 2, 4, 2, 2, or 5 if the clinical sign is present (Love et al., 2014). If a calf's total score is >5, the calf is considered positive for respiratory disease (Love et al., 2014). It should be noted a temperature score is only necessary if the other clinical signs total to less than 5 (Love et al., 2014).

Though two clinical scoring systems exist, this review will be focusing on the Wisconsin Calf Health Scoring System (McGuirk and Peek, 2014). In addition to CRS, the Wisconsin Calf Health Scoring system includes an attitude score, navel score, joint score, and fecal score (McGuirk and Peek, 2014). The attitude score ranges from 0-3 and is defined as: 0 = bright, alert, responsive; 1 = dull but responds to stimulation; 2 = depressed, slow to stand or reluctant to lie down; and 3 = unresponsive to stimulation (Wisconsin Calf Health Scoring App; https://www.vetmed.wisc.edu/dms/fapm/apps/chs.htm). The navel score ranges from 0-3 and is defined as: 0 = normal; 1 = slightly enlarged, not warm or painful; 2 = slightly enlarged with slight pain or moisture; and 3 = enlarged with pain, heat or malodorous discharge (McGuirk, 2008). The joint score ranges from 0-3 and is defined as: 0 = normal; 1 = slight swelling, not warm or painful; 2 = swelling with pain or heat, slight lameness; and 3 = swelling with severe heat, pain and lameness (McGuirk, 2008). The fecal score ranges from 0-3 and is defined as: 0 = normal; 1 = semi-formed, pasty; 2 = loose, but stays on top of bedding; and 3 = watery, sifts through bedding (McGuirk, 2008).

Ultrasound is a noninvasive diagnostic technique that can be performed quickly on farm to identify pneumonia, seen as non-aerated lung on an ultrasound, antemortem (Ollivett and

Buczinski, 2016). Pneumonia develops as a result of cellular infiltrates successfully displacing air from lung tissue (Ollivett and Buczinski, 2016). Ultrasound allows for continual monitoring of changes to lung tissue and provides caretakers with a real-time picture of a calf's lungs to assess disease progression or recovery. Lung ultrasound can be performed according to Ollivett and Buczinski (2016) using a rectal linear probe and portable ultrasound machine to evaluate the left and right lungs. Ollivett and Buczinski (2016) describe an ultrasound of the left lung as follows: begin scanning at intercostal space 6 corresponding to left caudal lung lobe, intercostal spaces 5-4 corresponding to the caudal aspect of the left cranial lung lobe, and intercostal spaces 3-2 corresponding to the cranial aspect of the left cranial lung lobe and of the right lung as follows: begin scanning at intercostal space 6 corresponding to the right caudal lung lobe, intercostal space 5 corresponding to the right middle lung lobe, intercostal spaces 4-3 corresponding to the caudal aspect of the right cranial lung lobe, and intercostal spaces 2-1 corresponding to the cranial aspect of the right cranial lung lobe. Lung ultrasound scores range from 0-5 and are defined as follows: 0 = normal lung, 1 = diffuse comet-tails, 2 = lobular pneumonia: consolidation $\geq 1cm^2$, 3 = lobar pneumonia: 1 entire lung lobe consolidated, 4 = lobar pneumonia: 2 entire lung lobes consolidated, and 5 = lobar pneumonia: ≥ 3 lung lobes consolidated (Ollivett and Buczinkski, 2016; Cramer and Ollivett, 2019). An ultrasound score ≥ 2 is considered abnormal and makes a calf eligible for treatment (Ollivett and Buczinski, 2016; Cramer and Ollivett, 2019).

Lung ultrasound is a highly accurate diagnostic tool to detect pneumonia (Ollivett et al., 2015; Ollivett and Buczinski, 2016). In Cuevas-Gómez et al. (2021), 61% of calves that were identified with clinical signs of respiratory disease had been identified with lung lesions an average of 10.5 days before clinical signs presented. Overall, 28% of calves in Cuevas-Gómez et al. (2021) were identified with subclinical respiratory disease that would have gone undetected without the use of lung ultrasound and therefore untreated. Lung ultrasound has been reported to have a sensitivity of 85% and a specificity of 98% in Holstein calves up to five months of age with various stages of clinical bronchopneumonia, lung abscess, and/or pneumothorax when compared with postmortem examinations (Rabeling et al., 1998). Additionally, Ollivett et al. (2015) assessed the accuracy of lung ultrasound and bronchoalveolar lavage fluid as antemortem respiratory disease identification tools. Ollivett et al. (2015) reported a sensitivity of 94% and specificity of 100% for lung ultrasound compared to post-mortem examinations. Additionally, the presence of abnormal, or non-aerated (Reef et al., 2004), lung tissue increased a calf's risk for having a bronchoalveolar lavage fluid neutrophil proportion $\geq$4% (Ollivett et al., 2015). The sensitivity and specificity of lung ultrasound may vary between studies due to the definition of pneumonia used, as well as the lung ultrasound techniques (i.e., the intercostal spaces evaluated), and comparison method utilized.

Lung ultrasound is advantageous in accurately identifying subclinical cases of pneumonia, but there are important considerations to consider for implementation on dairy farms as a disease detection tool (Ollivett and Buczinski, 2016). For example, lung ultrasonography requires veterinarian oversight and ultimately more labor and time to train personnel and perform the exam. Despite the barriers to implementation, lung ultrasonography is the most sensitive pre-mortem respiratory disease detection tool and enables earlier disease detection as well as captures subclinical cases of pneumonia (Ollivett et al., 2015; Ollivett and Buczinski, 2016).

1.3 Treatment

A key factor in managing respiratory disease is the actual treatment. According to producer-reported data, 94.8% of preweaned heifers identified with respiratory disease are treated with an antimicrobial (USDA, 2014). The two most commonly used classes of antibiotics for respiratory disease in preweaned heifers are florfenicol and macrolides (USDA, 2014). On average, veterinarians report administering 2 antimicrobial courses to a typical case of respiratory disease in calves before they consider the case resolved (Mijares et al., unpublished). In addition to antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs) have been evaluated as an ancillary therapy for their anti-pyretic and anti-inflammatory properties (Bednarek et al., 2003; Guzel et al., 2010; Lockwood et al., 2003; Mahendran, 2020). Though NSAIDs do not kill bacteria or prevent bacterial proliferation like antibiotics; NSAIDs have antipyretic, analgesic, and anti-inflammatory properties (e.g., pyrexia; Lockwood et al., 2003) and may have a supportive role in treating respiratory disease. Some NSAIDs (carprofen, diclofenac sodium, flunixin meglumine, ketoprofen, and meloxicam) have been studied as ancillary therapies for respiratory disease in cattle (Bednarek et al., 2003; Guzel et al., 2010; Lockwood et al., 2003; Mahendran, 2020). Bednarek et al. (2003) utilized clinical signs of disease to identify respiratory disease (fever, cough, nasal discharge, dyspnea, anorexia and apathy) and upon identification of respiratory disease, assigned calves to one of three treatment groups: oxytetracycline (administered intramuscularly), oxytetracycline with meloxicam (administered intravenously), or oxytetracycline with flumethasone (administered intravenously). Bednarek et al. (2003) then observed calves for the next 5 days and measured clinical signs of disease. Ultimately, significant improvement in body temperature and clinical scores were observed in calves that received intravenous meloxicam and oxytetracycline compared to calves in the other two treatment groups, suggesting a therapeutic effect on fever and clinical scores of meloxicam as an ancillary therapy to oxytetracycline in calves with respiratory disease (Bednarek et al., 2003). Additionally, Guzel et al. (2010) compared intramuscular diclofenac sodium and intravenous flunixin meglumine as ancillary therapies to subcutaneous tulathromycin in 80 holstein calves identified with respiratory disease using a clinical score described by Balmer et al. (1997). Calves were given a clinical score on the day of treatment and on days 1, 2, 3, 7, and 14 following treatment (Guzel et al., 2010). Similar to Bednarek et al. (2003), Guzel et al. (2010) reported significant improvement in pyrexia and respiratory rate in calves that received either NSAID compared to calves that only received the antibiotic. The effects of diclofenac sodium and flunixin meglumine on clinical signs of disease were not significant beyond 48 hours (Guzel et al., 2010). Lockwood et al. (2003) compared the effects of a single dose of flunixin meglumine (2.2 mg/kg by intravenous injection), ketoprofen (3 mg/kg by intravenous injection), or carprofen (1.4 mg/kg by subcutaneous injection) as ancillary therapies to ceftiofur (1.1 mg/kg for three days administered subcutaneously) for respiratory disease to treatment with ceftiofur alone. Respiratory disease was defined as a fever of at least 40°C and an illness score indicating at least moderate illness or at least moderate dyspnea, in mixed-breed beef cattle at 2, 4, 6, 12, 24, 48, and 72 hours after treatment (Lockwood et al., 2003). Like Guzel et al. (2010), Lockwood et al. (2003) observed a significant effect of NSAID on pyrexia reduction shortly after treatment (24 hours). In addition to clinical results, Lockwood et al. (2003) performed post-mortem examinations and reported significantly less lung consolidation in calves treated with flunixin meglumine and ceftiofur than calves that received any other combination of an NSAID and/or ceftiofur.

Another study evaluated the effects of only providing an NSAID (flunixin meglumine), compared to only an antibiotic (gamithromycin), in 83 calves identified with respiratory disease (Mahendran et al., 2017). Respiratory disease was defined as a sustained ear canal temperature of ≥39.7°C for six hours and absence of other disease (Mahendran et al., 2017). Calves that received only flunixin meglumine were five times more likely to have a fever 72 hours after initial treatment and required treatment with the antibiotic compared to calves that received gamithromycin at the initial treatment (Mahendran et al., 2017). In a second study by Mahendran (2020), respiratory disease was also defined as a temperature of ≥39.7°C exclusion of other disease using the Wisconsin Calf Health Score. A lung ultrasound was performed within 48 hours of and 14 days following treatment (Mahendran, 2020). Upon identification, calves were randomly assigned to one of three treatment groups: flunixin meglumine only, florfenicol only, or flunixin meglumine with florfenicol (Mahendran, 2020). Like Mahendran et al. (2017), Mahendran (2020) concluded that calves given an NSAID only required more treatments due to fever reoccurrence than calves that received an antibiotic supporting the potential role of NSAIDs as ancillary therapies to antibiotics and not a sole method of treatment for respiratory disease. Koster et al. (2021) identified respiratory disease in commercial beef and dairy cattle using the criteria of a rectal temperature ≥ 40.0°C, respiration score 2 or 3 and depression score 2 or 3 (specific to the study). Upon identification, cattle were randomly assigned to receive either a single subcutaneous injection of tulathromycin-ketoprofen or tulathromycin (Koster et al., 2021). Calves that received tulathromycin-ketoprofen experienced significantly faster reduction in rectal temperature in the first 24 hours following treatment and faster improvement in respiration rate and depression score compared to calves that only received tulathromycin (Koster et al., 2021). Overall, research has shown that providing calves or cattle with an NSAID as an ancillary therapy to an antibiotic for respiratory disease usually results in faster reduction of fever and clinical signs of disease in the first few days following treatment compared to calves that receive an antibiotic alone or an NSAID alone. However, the methods utilized in existing studies are not directly comparable as studies included populations of different ages of cattle, utilized different definitions of respiratory disease, measured the effects of treatment at different timepoints, and administered different combinations of an NSAID and antibiotic. For example, Mahendran (2020) and Lockwood et al. (2003) both assessed the effect of flunixin meglumine on lung consolidation, but Mahendran (2020) compared flunixin meglumine only, florfenicol only, or flunixin meglumine with florfenicol and Lockwood et al. (2003) compared flunixin meglumine as an ancillary therapy to ceftiofur compared to ceftiofur alone. Mahendran (2020) performed lung ultrasounds 48 hours and 14 days after treatment whereas Lockwood et al. (2003) performed post-mortem examinations 1-2 days after treatment and the studies reported different effects of flunixin meglumine on lung consolidation: Lockwood et al. (2003) observed significantly less lung consolidation in calves treated with flunixin meglumine and ceftiofur and Mahendran (2020) observed no effect between treatment groups likely explained by the differences in measurements and treatments.

One ancillary therapy that has not been previously studied in preweaned calves with respiratory disease is oral meloxicam. Pyrexia and inflammation are common characteristics of respiratory disease (McGill and Sacco, 2020), that may be painful (Ferreira, 1983), and NSAIDs, such as oral meloxicam, should be investigated for the potential to relieve these negative effects of disease through anti-inflammatory, analgesic and antipyretic mechanisms. Meloxicam preferentially inhibits the isoenzyme cyclo-oxygenase-2 that is produced in response to inflammatory stimuli, prohibiting the production of prostaglandins (Lees, 2009; Mosher et al., 2011). By preferentially binding to COX-2, meloxicam should not inhibit COX-1 therefore reducing the risk of impaired gastric and renal function (Day and Graham, 2004). However, meloxicam can still have negative effects on the renal, gastrointestinal, and vascular system though reduced compared to non-selective COX inhibitors (Berkowitz et al., 2021; Davies and

Skjodt, 1999). In addition, oral meloxicam is an appealing treatment for respiratory disease for its reasonable cost of $0.30/100 kg compared to intravenous meloxicam at $58.00/100 kg (Coetzee et al., 2009) and its ease of administration compared to an intravenous injection. Though oral meloxicam has not been studied for the treatment of respiratory disease, it has been evaluated extensively as a method of pain mitigation for castration and dehorning in cattle (Allen et al., 2013; Olson et al., 2016).

1.4 AMDUCA relative to ADG and the change in attitude, clinical respiratory, and lung ultrasound scores in calves with respiratory disease

The Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA) legalized the extralabel use of FDA approved drugs under direct guidance of a licensed veterinarian within the context of a veterinarian-client-patient relationship. Currently, analgesics are not approved for the purpose of preserving ADG during illness or improving attitude, clinical respiratory, or lung ultrasound scores in livestock in the United States (Compendium of Veterinary Products, 2010). Average daily gain is of interest to producers, and therefore an important aspect to investigate because weight is an indicator of animal health and is associated with production (Chester-Jones et al., 2017; Soberon et al., 2012).

Research has reported both an association between NSAIDs and increased weight gain following painful procedures (Faulkner and Weary, 2000; Coetzee et al., 2012; Glynn et al., 2013) as well as no effects on ADG when providing an NSAID (Coetzee et al., 2011; Stock et al., 2021). However, literature evaluating the effects of NSAIDs on ADG associated with respiratory disease is limited, but calves with respiratory disease gain less weight than calves without (Cramer and Ollivett, 2019) and there is a need for therapy to reduce the effects on ADG and ultimately a calf’s biological function.

As there are no approved drugs for the purpose of preserving ADG and improving attitude, clinical and lung ultrasound scores, analgesics can only be administered in this way in an extra-label drug use (ELDU) manner under the guidance of a veterinarian according to the American Medicinal Drug Use Clarification Act of 1994 (AMDUCA, 1994). A calf's attitude can be used as an indicator of recovery following treatment and aid in the ability to gauge recovery and determine if retreatment is required (Cantor et al., 2022). Additionally, monitoring of clinical signs of disease and performance of lung ultrasonography following treatment can aid in measuring the progression in severity or resolution of disease and retreatment decisions (Binversie et al., 2020; Jourquin et al., 2022) There is a lack of approved therapies for minimizing weight loss and improving attitude, clinical, and lung ultrasound scores in calves with respiratory disease. Average daily gain is an important indicator of health and associated with future production, therefore important to preserve during disease (Krpálkvoá et al., 2014). Attitude, clinical respiratory, and lung ultrasound scores can be used to monitor disease severity and duration and inform management decisions, therefore it is important to assess the effects of NSAIDs on these measurements. The lack of approved ancillary therapies for these purposes and the unchanging mortality due to respiratory disease presents an opportunity to investigate additional therapies to reduce negative effects of disease and improve health outcomes.

1.5 Investigation of meloxicam in painful procedures

Little to no literature exists regarding the use of oral meloxicam in the treatment of respiratory disease but we can conclude from other studies that meloxicam has been effective at reducing pain and inflammation in calves following painful procedures (Glynn et al., 2013; Heinrich et al., 2009; Heinrich et al., 2010; Olson et al., 2016). Overall, the administration of meloxicam as pain mitigation in painful procedures, such as dehorning and castration, is associated with lower heart rates, lower pain scores on a visual analog scale, lower plasma cortisol and substance P concentrations, greater motion indexes and number of steps, less lying time and lying bouts, less frequent pain behaviors (e.g., ear flicking) and improved ADG (Glynn et al., 2013; Heinrich et al., 2009; Heinrich et al., 2010; Olson et al., 2016. Furthermore, meloxicam has also been associated with a reduction in scrotal inflammation 3 days following surgical castration in calves compared to calves that received a placebo (Olson et al., 2016).

Although research regarding pain associated with respiratory disease in calves is in its infancy, existing research does provide evidence that respiratory disease is painful (Martin et al., 2022). More research is needed to better characterize and define how painful respiratory disease is and identify appropriate treatment methods. Since meloxicam has been shown to be safe and effective at relieving pain post-castration and cautery dehorning (Glynn et al., 2013; Heinrich et al., 2009; Heinrich et al., 2010; Olson et al., 2016), it is worthwhile to consider its ability to relieve pain and decrease inflammation associated with respiratory disease.

1.6 Gaps in knowledge and future direction

Despite extensive knowledge of the pathogenesis of respiratory disease and advanced diagnostic tools, respiratory disease continues to be one of the leading causes of morbidity and mortality in preweaned calves (USDA, 2018). Researchers have begun investigating the efficacy of NSAIDs as an ancillary therapy to an antibiotic for respiratory disease, but methods and results between studies have varied. The inconclusive results justify the need for continued investigation of NSAIDs in the treatment of respiratory disease across various commercial settings to identify factors aiding or impeding their efficacy. Specifically, there is limited data available regarding the effects of NSAIDs as ancillary therapies on growth associated with respiratory disease, or changes in attitude, clinical and lung ultrasound scores. Though lung ultrasonography is not commonly used on dairy farms today, it is an accurate, noninvasive tool to identify pneumonia and detect subclinical cases of disease that growth, attitude, and clinical scores may not detect. Future research should aim to compare growth associated with respiratory disease in calves treated with and without an NSAID in addition to an antibiotic and the effects on attitude, clinical and lung ultrasound scores in the short and long term.

1.7 Conclusion

Overall, the use of NSAIDs as an ancillary therapy to an antibiotic in preweaned dairy calves is not yet fully understood and the therapies available are limited. Respiratory disease affects a calf's growth and future production and accounts for a significant proportion of calf mortalities, therefore it is important to continue investigation into improved management practices. Research has shown that NSAIDs are associated with reduction in body temperature in the first 48 hours following treatment, but there is mixed data regarding the effect NSAIDs have on growth and the effects of oral meloxicam on ADG in calves with respiratory disease has not been previously reported. The effects of NSAIDs on attitude, clinical respiratory, and lung ultrasound scores in calves with respiratory disease have been mixed likely due to differences in study methods, but NSAIDs have anti-inflammatory properties that make them a candidate to relieve negative effects of disease and should continue to be investigated as ancillary therapies. Further research should assess the effects of NSAIDs on calf growth, the change in attitude, clinical respiratory and lung ultrasound scores in the short and long term to determine consistent effects and identify treatment methods that are practical to implement in commercial settings in preweaned dairy calves.

CHAPTER 2: ASSESSING THE EFFECTS OF ORAL MELOXICAM AS AN ANCILLARY THERAPY GIVEN AT THE TIME OF RESPIRATORY DISEASE IDENTIFICATION ON GROWTH AND CHANGE IN CLINICAL AND ULTRASOUND SCORES IN PREWEANED DAIRY CALVES[1]

2.1 Introduction

In 2014, producer reported data collected through the National Animal Health Monitoring Service (NAHMS) estimated that respiratory disease affected 11.2% of preweaned dairy heifers and accounted for 24% of deaths (USDA, 2018). Respiratory disease develops through a complex interaction between the host's immune response, stressors, and pathogens (McGill and Sacco, 2020; Poulsen and McGuirk, 2009). A calf's immune system responds to pathogens by launching defense mechanisms (e.g., mucocilliary action, secretion of proinflammatory cytokines, secretion of neutrophils, etc.) that result in inflammation in the respiratory tract (McGill and Sacco, 2020). Clinical signs of disease that may be exhibited in response include nasal discharge, ocular discharge, cough, and a fever (McGuirk and Peek, 2014). Pathogens can invade the lower airway resulting in inflammation and lung tissue destruction, or pneumonia (McGill and Sacco, 2020). Early detection and intervention are key factors in preventing disease progression, which can be monitored by the severity of clinical signs of disease or lung ultrasound scores over time (Ollivett and Buczinski, 2016). Animals experiencing disease may exhibit behavioral changes, or sickness behaviors, such as lethargy, decreased grooming, appetite, or exploratory behaviors that may be collectively represented through assigning an

[1] Ferree, L.A., L.N Edwards-Callaway, I.N. Roman-Muniz, J.F. Coetzee, T. Applegate, T. Ollivett, M.C. Cramer

attitude score (Hart, 1988; Cramer and Stanton, 2015; McGuirk and Peek, 2014). Respiratory disease can further impact a calf by reducing average daily gain (Francoz et al., 2012). Previous studies have reported an association between respiratory disease and reduced average daily gain in preweaned calves (Cramer and Ollivett, 2019; Cuevas-Gómez et al., 2021), which likely partially explains the reduced first lactation milk production observed in calves with respiratory disease (Dunn et al., 2018).

According to NAHMS (2014), 94.8% of calves identified with respiratory disease are treated with an antimicrobial. However, despite treatment with an antimicrobial, mortality due to respiratory disease in preweaned heifers has remained relatively unchanged over the last 20 years, ranging from 21.3 - 24.0% (NAHMS, 2002; NAHMS, 2007; USDA, 2018). Furthermore, veterinarian respondents in a recent survey reported administering an average of 2 courses of antimicrobial treatment in a typical case of respiratory disease before clinical signs resolved, suggesting that a single antimicrobial course is not always effective (Mijares et al., unpublished). Unchanged trends in mortality due to respiratory disease and the need for repeated treatments highlight the need to further investigate effective treatment methods for respiratory disease in preweaned dairy calves.

Non-steroidal anti-inflammatory drugs (NSAIDs) have been recommended as ancillary therapies in affected animals to reduce the severity of clinical signs of disease, increase appetite, and decrease inflammation-induced lung damage (Francoz et al., 2012). Currently, there is not an NSAID labeled for minimizing weight loss associated with respiratory disease and there are no studies reporting an association between improved average daily gain and the administration of an NSAID following respiratory disease identification in preweaned dairy calves (Francoz et al., 2012). The effects of NSAIDs on ADG associated with respiratory disease can be investigated via extra label drug use (ELDU) with veterinarian approval under the Animal Medicinal Drug Use Clarification Act (AMDUCA, 1994). Calves with respiratory disease in the preweaning period gain less weight than calves that are unaffected (Cramer and Ollivett, 2019; Cuevas-Gómez et al., 2021) and calves with higher preweaned average daily gain are more likely to produce more milk later in life (Soberon and Amburgh, 2013). A study in cattle with respiratory disease reported a greater ADG at 70, 105, and 172 days following treatment with meloxicam and oxytetracycline compared to cattle that received a placebo and oxytetracycline (Friton et al., 2005) providing evidence that meloxicam may be beneficial in long term weight gain in affected animals. There is a need for therapies to minimize reductions in ADG associated with respiratory disease because of the impacts of respiratory disease on ADG, which can affect long-term productivity.

Furthermore, there are no NSAIDs labeled for improving attitude, clinical respiratory or lung ultrasound scores, which would also be considered ELDU and requires veterinarian approval and oversight under AMDUCA (1994). Two recent studies investigating NSAIDs as ancillary therapies for respiratory disease reported no association between an NSAID and calves' attitude (Koster et al., 2021; Mahendran. 2020). A systematic review reported the only consistent finding associated with the addition of an NSAID to be a reduction in fever in the early follow-up period compared to an antimicrobial alone, but no association between a clinical respiratory score and NSAIDs were reported (Francoz et al., 2012). Lockwood et al. (2003) performed post-mortem lung examinations 2-3 days after treatment in beef cattle and Friton et al. (2005) examined beef cattle's lungs at slaughter, over 105 days after treatment. The reduction in lung consolidation was attributed to flunixin meglumine in Lockwood et al. (2003) and meloxicam in Friton et al. (2005). Improvement in attitude, clinical respiratory, or lung ultrasound scores would indicate treatment success and a reduction in the negative effects of disease a calf was experiencing, therefore improving the calf's ability to cope with and recover from respiratory disease. Because of the negative effects of disease a calf experiences and unchanging mortality, the need for continued investigation of disease management is warranted.

To our knowledge, oral meloxicam has not yet been evaluated as an ancillary therapy for its effects on ADG, attitude, clinical respiratory, or lung ultrasound scores in preweaned dairy calves but has been reported to alleviate pain and inflammation associated with painful procedures such as castration and disbudding (Wagner et al., 2021). Meloxicam is an NSAID with antipyretic and analgesic properties that may aid in alleviating inflammation associated with respiratory disease (McGill and Sacco, 2020) and ultimately aid in minimizing the reduction in ADG and improve attitude, clinical respiratory, and lung ultrasound scores. The desired target of meloxicam is an isoform of the enzyme cyclo-oxygenase (COX), known as COX-2 which is upregulated in response to inflammatory stimuli (Lees, 2009; Mosher et al., 2012). Meloxicam acts by preferentially inhibiting the production of COX-2, preventing or reducing the production of prostaglandins, key mediators in the inflammatory and pain response (Mosher et al., 2012).

A study in feedlot heifers evaluated a single subcutaneous injection of meloxicam as an ancillary therapy to an antibiotic for respiratory disease diagnosed by a veterinarian based on clinical signs of disease and a rectal temperature $\geq$40.0°C (Friton et al., 2005). Friton et al. (2005) concluded that cattle that received meloxicam gained 0.11 kg/d more than heifers that received a placebo. Bednarek et al. (2003) reported a significantly faster improvement in body temperature in calves that received intravenous meloxicam as an ancillary therapy compared to calves that received flunixin meglumine as an ancillary therapy and calves that only received an antibiotic. Though shown to be effective at reducing body temperature in calves with respiratory disease, intravenous meloxicam can be costly to administer at $58.00/100 kg compared to oral meloxicam at $0.30/100 kg (Coetzee et al., 2009). The investigation of oral meloxicam is justified by the need for effective therapies to improve ADG, attitude, clinical, and ultrasound scores in calves with respiratory disease, the reported effectiveness of other forms of meloxicam, its reasonable cost and ease of administration. Therefore, the objectives of this study were to assess the efficacy of a single dose of oral meloxicam as an ancillary therapy to an antibiotic given at the time of respiratory disease identification on growth and change in attitude, clinical respiratory, and lung ultrasound scores in preweaned dairy calves in a commercial setting. We hypothesized that the administration of oral meloxicam as an ancillary therapy to an antibiotic would preserve growth as well as improve attitude, clinical, and ultrasound scores in preweaned calves with respiratory disease.

2.2 Materials and Methods

This study received approval from the Institutional Animal Care and Use Committee at Colorado State University (Fort Collins, CO; IACUC Protocol #1541).

Animals and Facilities

The study population consisted of both male and female Holstein, Jersey, and crossbred preweaned calves on a single commercial dairy in the western United States. Calves were enrolled in the study from March 2021 to November 2021. Calves were between 1-14 days of age at enrollment and observed until weaning (WEAN) at 40-56 days of age. Calves were housed in a group of approximately 2-7 calves for the first 1-7 days after birth before being transported across the dairy to an individual Calf-tel® or metal hutch (dependent on availability) until weaning. In the beginning of the study (March-May), hutches were bedded with corn stalks and towards the end of the study (June-December) hutches were bedded with sawdust. Calves were also fed according to the dairy protocol receiving 4 L of milk divided between two feedings via bottle each day until caretakers deemed the calf was large enough, through visual observation, to receive 6 L of milk in the same manner each day. Once moved to the individual hutches, calves had *ad libitum* access to calf starter and a water bucket that was checked daily and refilled as needed.

Blood sampling

Blood samples to measure serum total protein (STP) were collected in the group newborn pen or individual hutches in the first 7 days of life. Samples were collected using a plastic needle hub, needles (20G x 1”; Exelint International Co, Redondo Beach, CA), and 10 mL red-top vacutainer tubes (BD Vacutainer®, Franklin Lakes, NJ). The blood samples were stored on ice packs in a cooler for transportation from the farm to the lab then centrifuged at 3,000 rpm for 15 minutes. A disposable pipette was used to remove the serum and place 1-2 drops in a digital refractometer to measure STP as an indicator of passive transfer (MISCO Palm Abbe, Solon, OH)). The STP results were defined as quality scores according to Lombard et al. (2021): excellent = ≥6.2 g/dL; good = 5.8-6.1 g/dL; fair = 5.1-5.7 g/dL; poor = <5.1 g/dL.

Health exams

Respiratory disease was identified using a combination of clinical scoring (McGuirk and Peek, 2014) and lung ultrasound scoring (Ollivett and Buczinski, 2016). From enrollment to weaning or death, calves underwent twice weekly health exams (11.37 ± 3.25 (mean ± SD)) and weight estimations using a heart girth measurement (Nasco, Fort Atkinson, WI). Our study focused on the outcomes of the health exams at three timepoints: NEXT: the subsequent health exam 2-3 days after the first identification of respiratory disease; WEEK: the health exam 7 days after the first identification of respiratory disease; and WEAN: the health exam closest to weaning following the first identification of respiratory disease.

Similar to methods described by Binversie et al. (2020), most (95%) of the health exams were performed by the first author (LF) and senior author (MCC) performing the remainder. MCC trained LF in clinical scoring and lung ultrasound prior to the start of the study and regularly observed LF for consistency. All data was collected through the University of Wisconsin Calf Health Scorer iPad application (https://www.vetmed.wisc.edu/fapm/). The clinical respiratory score (CRS) ranged from 0-3 with 0 being normal and 3 being severely abnormal and included an evaluation of ear position, ocular discharge, nasal discharge, cough, and rectal temperature. In addition, an attitude, joint, navel, and fecal score were obtained on the same scale but not included in the CRS. A calf is considered to have a positive CRS (CRS+) if it received a score $\geq$2 in $\geq$2 CRS categories (McGuirk and Peek, 2014). A portable lung ultrasound with a rectal probe (Ibex Pro, E.I. Medical, Loveland, CO) was used to evaluate the left and right lungs beginning caudally and progressing cranially (Ollivett and Buzcinski, 2016). The left lung was scanned beginning at intercostal space (ICS) 6 over the left caudal lung lobe, then ICS 5 to ICS 4 over the caudal aspect of the left cranial lung lobe, then ICS 3 and ICS 2 over the cranial aspect of the left cranial lung lobe (Ollivett and Buzcinski, 2016). The right lung was scanned beginning at ICS 6 over the right caudal lung lobe, then ICS 5 over the right middle lung lobe, then ICS 4 and ICS 3 over the caudal aspect of the right cranial lung lobe, and then ICS 2 and ICS 1 over the cranial aspect of the right cranial lung lobe (Ollivett and Buczinski, 2016). Lung ultrasound was scored on a 6-point scale from 0-5 with 0 being normal, $\geq$2 being abnormal, and 5 being severely abnormal (Ollivett and Buczinski, 2016; Cramer and Ollivett, 2019). Each ultrasound score was defined as follows: 0 = normal; only normal lung present; 1 = normal; mostly normal lung with diffuse comet-tails; 2 = abnormal; lobular pneumonia: area of consolidation $\geq 1 cm^2$; 3 = abnormal; lobar pneumonia: area of consolidation = 1 entire lung lobe; 4 = abnormal; lobar pneumonia: area of consolidation = 2 entire lung lobes; 5 = abnormal; lobar pneumonia: area of consolidation = ≥ 3 entire lung lobes (Ollivett and Buczinkski, 2016; Cramer and Ollivett, 2019). The additional measurements in the health exam were defined on the 4 point scale of 0-3, but not included in the CRS (McGuirk and Peek, 2014). The attitude score was defined as: 0 = bright, alert, and responsive; 1 = dull presentation but calf responds to stimulation; 2 = depressed presentation and calf is hesitant to lie down or slow to stand in response to stimulation; 3 = depressed presentation and calf is not responsive to stimulation (Wisconsin Calf Health Scoring App; https://www.vetmed.wisc.edu/dms/fapm/apps/chs.htm). The navel score was assigned through a physical evaluation of the navel for heat, swelling, or discharge and defined as: 0 = normal presentation; no heat, swelling, discomfort, or discharge; 1 = navel is slightly enlarged but is not warm or causing discomfort; 2 = navel is slightly enlarged, and calf exhibits some discomfort or discharge; and 3 = navel is obviously swollen with heat and/or discharge and discomfort (McGuirk, 2008). The fecal score was determined through visual and physical evaluation of a calf's feces and defined as: 0 = normal consistency; 1 = semi-formed on bedding but pasty; 2 = loose consistency but does not sift through bedding; 3 = watery consistency and sifts completely through bedding (McGuirk, 2008).

Treatment allocation and observer blinding

Once all calves under observation had received their health exam, the observer utilized both the CRS and lung ultrasound scores to identify the presence and type of respiratory disease. In the present study, respiratory disease was classified at first identification using three categories: upper respiratory tract infection (URT) = calf was CRS+ with a normal ultrasound score; subclinical pneumonia (SCP) = calf was CRS- with an abnormal ultrasound score; and clinical pneumonia (CP) = calf was CRS+ with an abnormal ultrasound score (Cramer and Ollivett, 2019).

Upon first identification of respiratory disease, calves received Tulathromycin (Draxxin at 1.1 mL/kg once subcutaneously) according to the existing farm protocol and were randomly allocated to a treatment group: oral meloxicam (MEL; 1 mg/kg) or placebo (PLA: lactose monohydrate in a gelatin capsule; 1 mg/kg). Calves were randomly allocated using a predetermined randomized list generated in Microsoft Excel (Microsoft Corp., Redmond, WA) using the random number function and creating blocks of 10 by respiratory disease type (URT, SCP, CP) to ensure equal distribution among treatment groups and respiratory disease type.

To prevent observer bias, the observer performing health exams was blinded to treatment group allocation for the entirety of the study until completion of statistical analyses. Members of the research team maintained records of all treatments administered including the calf's identification number, date of administration, type of respiratory disease identified, name of drug administered, dosage administered, the name of the researcher that calculated the dosage, and the name of the researcher that administered the drug. Drug dosage was calculated based on the estimated weight from the heart girth measurement collected at the health exam at time of allocation (Binversie et al., 2020). The observer performing health exams did not have access to the treatment records stating the name of the drugs given but instead "A" and "B" were used in place of MEL or PLA to label treatment group for analyses. The observer was also not involved in the calculation or administration of MEL or PLA. Farm personnel agreed to report any treatments they administered to calves enrolled in the trial and farm records were used to determine calves that died during the trial.

Statistical analysis

All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC). The experimental unit was the calf. Prior to the start of the trial, a sample size calculation was performed with average daily gain (ADG) as the outcome of interest. The calculation determined 80 calves per treatment group were needed, so the sample size was inflated by 25-35% to account for any death and loss to follow-up that may have occurred. Therefore, our goal was to enroll approximately 100-108 calves per treatment group with ≥80 calves remaining in each group in the final analyses. The predictor of interest in this trial was treatment group (MEL vs. PLA), so the final analyses only included calves that were identified with respiratory disease (URT, SCP, or CP) and received MEL or PLA in addition to Tulathromycin. The categorical variables evaluated as potential confounders included: sex (male; female), breed (Holstein; Jersey; Crossbreed), season born (0 = Feb-March; 1 = April-May; 2 = June-July; 3 = August-September; 4 = October-November), respiratory disease type at first identification (URT; SCP; CP), quality of passive transfer ((excellent = ≥6.2 g/dL; good = 5.8-6.1 g/dL; fair = 5.1-5.7 g/dL; poor = <5.1 g/dL; Lombard et al., 2021), navel (yes = at least one score ≥2 during observation; no = never had a navel score ≥2), diarrhea (yes = one score ≥3 during observation; no = never had a fecal score ≥3). The continuous variables evaluated as potential confounders included: the number of days a calf was observed following the first identification of respiratory disease, the calf's age in days at time of first respiratory disease identification, and the calf's weight at their first health exam calculated using the heart girth measurement (Davis et al., 1961). The potential confounders were evaluated using Spearman's correlation, logistic regression, Wilcoxon ranksum test, Fisher's exact test, or chi-square analysis depending on each variable type. A variable was considered associated with the outcome of interest at $P < 0.2$ and offered to the full model for further analysis.

Outcomes

Average daily gain following first identification of respiratory disease until weaning or death was the primary outcome of interest in the present study. The ADG (kg/d) was calculated using a linear regression (PROC REG) with the calf's age and converted heart girth measurement (Davis et al., 1961) from each health exam. The health outcomes assessed at NEXT and WEEK were: attitude (0 = normal or not depressed; 1 = depressed; https://www.vetmed.wisc.edu/dms/fapm/apps/chs.htm; Cramer and Ollivett, 2019); CRS (0 = CRS-; 1 = CRS+; McGuirk and Peek, 2014); and abnormal ultrasound score (0 = normal or ultrasound score <2; 1 = abnormal or ultrasound score ≥2; Ollivett and Buczinski, 2016; Cramer and Ollivett, 2019). A single outcome was assessed at WEAN: respiratory disease status (0 = no respiratory disease at weaning; 1 = URT, SCP, or CP at weaning).

Models

For each model, the predictor of interest was treatment group and no confounding variables were identified. To test the effect of treatment group on ADG, a mixed linear model (PROC MIXED) was used and included an LSMEANS statement to produce estimates ± SEM for ADG by treatment group. Outliers were assessed using studentized residual plots. The effect of treatment group on the proportion of calves in MEL and PLA with a depressed attitude, CRS+, and abnormal ultrasound score at NEXT and WEEK were assessed using a logistic model

(PROC GLIMMIX). The effect of treatment group on respiratory disease status at WEAN was assessed using a logistic model (PROC GLIMMIX).

2.3 Results

A total of 215 calves were allocated to treatment group (MEL: n = 107; PLA: n = 106) but 11.6% (25/215) were excluded from analysis for the following reasons: loss to follow-up due to management decisions to move calves elsewhere on the dairy before weaning (MEL = 2; PLA = 3), lameness (MEL = 4; PLA = 0), maggot infestation (MEL = 1; PLA = 0), were not treated at the first identification of respiratory disease but rather at a subsequent identification due to human error (MEL = 2; PLA = 0), were improperly identified (MEL = 2; PLA = 1), received a second round of treatment (MEL = 3; PLA = 6), or received the incorrect NSAID treatment from what was assigned (MEL = 1; PLA = 0) leaving 190 calves eligible for final analysis. The sample size at each time point varied due to incomplete data and is presented with the results. One hundred and eighty-nine calves had complete ADG data but 2 outliers were removed, so 187 calves were included in the ADG analysis. One hundred and eighty-one calves were included at NEXT (Table 1), 165 at WEEK (Table 1), and 155 at WEAN (Table 1). Random allocation was successful as evidenced by the distribution of respiratory disease type between treatment groups in the calves included in ADG analysis (P = 0.9729), as well as the calves included in each timepoint: NEXT (P = 0.8481), WEEK (P = 0.7260), and WEAN (P = 0.7771).

Table 1. Number of calves per treatment group at NEXT (n=181), WEEK (n=165), and WEAN (n=155) by respiratory disease type at first identification

	NEXT	*NEXT*	*WEEK*	*WEEK*	*WEAN*	*WEAN*
Type of respiratory disease at first	**Meloxicam (n=number of calves)**	**Placebo (n=number of calves)**	**Meloxicam (n=number of calves)**	**Placebo (n=number of calves)**	**Meloxicam (n=number of calves)**	**Placebo (n=number of calves)**

identification						
Upper respiratory tract infection[2]	43	50	38	45	35	44
Subclinical pneumonia[3]	36	35	35	32	32	32
Clinical pneumonia[4]	8	9	7	8	6	6
Total	87	94	80	85	73	82

Average daily gain

The effect of treatment group was not associated with ADG (P = 0.7139). The ADG for calves that received MEL was 0.54 ± 0.11 (mean ± SEM) kg/day compared to 0.57 ± 0.10 kg/day in the PLA group.

Attitude, clinical respiratory score, and ultrasound at NEXT and WEEK

The effect of treatment group was not associated with attitude (P = 0.1053; Table 2), CRS (P = 0.3154; Table 2), or abnormal ultrasound score (P = 0.2842; Table 2) at NEXT. The effect of treatment group was not associated with attitude (P = 0.4552; Table 2), CRS (P = 0.6910; Table 2), or abnormal ultrasound score (P = 0.9494; Table 2) at WEEK.

Table 2. Results for calves at NEXT (n=181) and WEEK (n=165) that were identified with respiratory disease

	NEXT	*NEXT*	*NEXT*	*WEEK*	*WEEK*	*WEEK*
Outcome	**Meloxicam**	**Placebo**	**P-value**	**Meloxicam**	**Placebo**	**P-value**
Depressed attitude[5]	20.7% (18/87)	11.7% (11/94)	0.1053	6.3% (5/80)	9.4% (8/85)	0.4552

[2] CRS+ and ultrasound score of 0 or 1
[3] CRS- and ultrasound score $\geq$2
[4] CRS+ and ultrasound score $\geq$2
[5] Attitude score $\geq$2

CRS+[6]	12.6% (11/87)	18.1% (17/94)	0.3154	8.75% (7/80)	10.6% (9/85)	0.6910
Abnormal lung ultrasound[7]	16.1% (14/87)	10.6% (10/94)	0.2842	27.5% (22/80)	27.1% (23/85)	0.9494

Respiratory disease status at WEAN

One hundred and fifty-five calves were included in the analysis at WEAN (Table 1). The effect of treatment group on respiratory disease status at WEAN was not significant (P = 0.8572; Table 3).

Table 3. Respiratory disease status at WEAN by treatment group (n=155)

Treatment group	Number of calves with respiratory disease at weaning	Number of calves without respiratory disease at weaning
Meloxicam	42.5% (31/73)	57.5% (42/73)
Placebo	43.9% (36/82)	56.1% (46/82)

Death

Twelve of the 215 calves allocated to a treatment group died during the study (MEL: n = 5; PLA: n = 7; Table 4). Of the 12 calves that died, 10 were identified with respiratory disease at the health exam prior to death and the remaining 2 had a fever and bloody stool.

[6] $\geq$2 CRS categories $\geq$2
[7] Ultrasound score $\geq$2

Table 4. Calves that died following respiratory disease identification by treatment group and respiratory disease type

Respiratory type at first respiratory identification	Meloxicam (n = number of calves that died)	Placebo (n = number of calves that died)
Upper respiratory tract infection	3	4
Subclinical pneumonia	2	2
Clinical pneumonia	0	1
Total	5	7

2.4 Discussion

To our knowledge, this clinical trial is the first of its kind to assess the effects of a single dose of oral meloxicam as an ancillary therapy to an antibiotic for respiratory disease in preweaned dairy calves. Similar to existing literature (Francoz et al., 2012), our results did not support an association between treatment group and growth, measured as ADG, or health, measured using attitude, CRS, and ultrasound scores. The outcomes of the present study may be reflective of management factors specific to the enrolled commercial farm, which provided realistic conditions for the trial.

Average daily gain

Average daily gain was not associated with treatment group in our trial, which is consistent with previous findings that NSAIDs are not associated with growth in calves with respiratory disease (Francoz et al., 2012). All calves in our study received 4-6 L of milk per day per the farm’s protocol. Rosadiuk et al. (2021) defined 4-6 L as a low plane of nutrition and it is possible that in the current study the amount of milk provided affected study outcomes. Calves on lower planes of nutrition have less energy to expend and calves enrolled in our study may have shifted more energy towards launching an immune response during respiratory disease and had minimal energy leftover to contribute to growth, or ADG (Ollivett et al., 2012). For example, calves with respiratory disease in Cramer and Ollivett (2019) received 5 L of milk twice per day and gained 0.21-0.30 kg/d more than calves in our study. Mahendran (2020) utilized TempVerified FeverTags to identify calves with respiratory disease through the identification of a fever and exclusion of other disease (e.g., navel or joint ill) and then treated sick calves with flunixin meglumine as an ancillary method to an antibiotic. The calves in Mahendran (2020) were also on a higher plane of nutrition and gained 0.11-0.12 kg/d more than calves in the present clinical trial. The association between plane of nutrition and the efficacy of NSAIDs as an ancillary therapy for respiratory disease has not yet been reported. However, NSAIDs have been shown to be more effective in calves on a higher plane of nutrition, defined as up to 15 L of milk per day, following disbudding compared to calves on a lower plane of nutrition (Reedman et al., 2022). The reason we did not observe an effect of treatment group in the present study is potentially explained by the reduced efficacy of NSAIDs on a lower plane of nutrition (Reedman et al., 2022) and calves' reduced ability to recover from disease on a low plane of nutrition (Ollivett, 2012). Plane of nutrition in calves varies based on a calf's body weight, energy requirements, and environmental conditions (i.e., temperature; Drackley, 2008) and should be further investigated as factors affecting the efficacy of NSAIDs on calf growth and health outcomes associated with respiratory disease.

Depressed attitude

A depressed attitude was not associated with treatment group at NEXT or WEEK in our trial. The half-life of meloxicam is 27 hours (Coetzee et al., 2009), therefore its effects on calf behavior may not have been observed at NEXT or WEEK that occurred between 48-72 hours or 7 days later. As observed in our study, no association between calf demeanor and the administration of an NSAID were observed by Mahendran (2020). Another study in cattle evaluated a combination of ketoprofen and tulathromycin as a treatment for respiratory disease and did not observe an association between treatment and attitude 3-14 days following drug administration (Koster et al., 2021). The ability to observe the effects of an NSAID may vary based on the timepoint observations are made post-administration. For example, Mintline et al. (2013) observed increased play behavior up to 3 hours post-disbudding in calves that received meloxicam but did not observe any behavior differences at 27 hours between calves that did and did not receive meloxicam. In Reedman et al. (2022), calves that received meloxicam had decreased pressure sensitivity up to 120 minutes following caustic disbudding compared to calves that did not receive meloxicam, but there were no observed differences in pressure sensitivity at 3-4 or 7 days following disbudding. Both Mintline et al. (2013) and Reedman et al. (2022) suggest the analgesic properties of meloxicam have been effective in the short-term in reducing pain associated with disbudding in dairy calves. Though we did not observe an association between NSAID and attitude in our study, more research is needed to evaluate the effects of meloxicam on behavior at timepoints within meloxicam's half-life.

Clinical respiratory score

Clinical respiratory score was not associated with NSAID at NEXT or WEEK. This contrasts with other studies that did report a difference in clinical signs of disease between treatment groups. Guzel et al. (2010) utilized a clinical index score like the clinical scoring system used in our study and did observe an improvement in clinical signs of respiratory disease in the first 48 hours in calves given diclofenac sodium or flunixin meglumine as an ancillary therapy to an antibiotic. Additionally, Bednarek et al. (2003) observed a significantly faster improvement in clinical signs of respiratory disease that was more pronounced in calves treated with meloxicam than calves that did not receive meloxicam 5 days following treatment. The scoring system used in the present study was designed to detect early signs of respiratory disease whereas the systems used in Bednarek et al. (2003) and Guzel et al. (2010) had definitions meeting more advanced respiratory disease such as dyspnea and a fever of 39.5°C that may explain the variance in results between studies. Like our study, Guzel et al. (2010) did not observe an effect of treatment on perceived recovery of disease at 7 days following treatment. Though we did not observe an effect of treatment group on clinical signs of disease, existing literature has suggested that providing an NSAID as an ancillary therapy for respiratory disease may aid in the reduced severity of clinical signs of disease in the first few days following treatment. Future research should investigate treatment protocols that may reduce the severity of clinical signs of disease beyond the first few days.

Ultrasound score

An abnormal ultrasound score was not associated with NSAID at NEXT or WEEK. Like the present study, Mahendran (2020) did not observe an effect of an NSAID as an ancillary therapy on lung ultrasound scores at 48 hours or 14 days following treatment administration. However, Lockwood et al. (2003) reported significantly less abnormal lung tissue in calves treated with flunixin meglumine compared to calves treated with an antibiotic alone through post-mortem examinations one to two days after treatment occurred. Conflicting data suggests the need for future research to determine the effects of providing oral meloxicam, or another

NSAID, as an ancillary therapy for respiratory disease on lung ultrasound scores at short and long term timepoints.

Respiratory disease status at WEAN

Like Binversie et al. (2020), we assessed a similar variable of respiratory disease status at WEAN. However, our study is not directly comparable to the methods in Binversie et al. (2020) as Binversie et al. (2020) compared the effects of an antibiotic in calves with respiratory disease to calves that did not receive an antibiotic, whereas all calves in our study received an antibiotic and we compared the effects of an additional therapy with an NSAID to a placebo. It is also possible we did not observe an effect of NSAID at WEAN due to the long duration between treatment and WEAN. A calf's state of disease at weaning is important to evaluate as calves with lung consolidation are less likely to get pregnant and more likely to be culled before their first parturition (Teixeira et al., 2-17), supporting a need for therapy to reduce the number of heifers with lung consolidation at weaning

However, studies with differing methods have reported an observed long-term association between NSAID and incidence of respiratory disease (Coetzee et al., 2012; Friton et al., 2005). Coetzee et al. (2012) reported a lower incidence of respiratory disease over a 28 day period in calves that received oral meloxicam (1 mg/kg) upon arrival to the feedlot and at time of castration compared to calves that did not receive oral meloxicam. Friton et al. (2005) reported observed benefits of administering meloxicam over a longer period of time: 3% fewer cattle had lung lesions at slaughter than those that did not receive meloxicam upon arrival to the feedlot. To the authors' knowledge, there are no studies reporting the effects of oral meloxicam on respiratory disease status at weaning in preweaned dairy calves. Given that Coetzee et al. (2012) and Friton et al. (2005) reported long term benefits of providing an NSAID on respiratory disease status, future research should continue evaluating the long term effects of oral meloxicam in dairy calves.

2.5 Conclusion

The objectives of the present study were to assess the efficacy of a one-time dose of oral meloxicam at time of respiratory disease identification as an ancillary therapy to an antibiotic on the health and performance of preweaned dairy calves in a commercial setting. To our knowledge, this study was the first to describe the effects of oral meloxicam as an ancillary therapy for respiratory disease in preweaned calves on growth and health. Though we did not observe an association of NSAID and growth or health, our study provided a basis for oral meloxicam used in an ELDU manner as an ancillary therapy to an antibiotic for its effects on growth and change in clinical and ultrasound scores in calves with respiratory disease in a commercial setting. Between our results and existing literature, we cannot definitively conclude the efficacy of oral meloxicam as an ancillary therapy to an antibiotic for respiratory disease in preweaned dairy calves and future trials should take place across various commercial settings to account for the influence of management factors and better describe the efficacy of oral meloxicam.

CHAPTER 3: ASSESSING THE EFFECT OF CASE-BASED TEACHING COMPARED WITH LECTURE-BASED TEACHING ON STUDENTS' KNOWLEDGE AND PERCEPTIONS IN A SENIOR UNDERGRADUATE DAIRY CATTLE MANAGEMENT COURSE[8]

3.1 Introduction

Traditional lecturing, a teaching method in which an instructor presents course content to students, is one of the predominant teaching methods utilized in higher education (Yuan et al., 2011; Roehl et al., 2013; Mesthrige et al., 2020). Lecture can be utilized to efficiently communicate large amounts of information to numerous students (Brown and Race, 2005; Charlton, 2006) and can reduce the cognitive load in students presented with new information by allowing students to focus on points emphasized by the instructor (Charlton, 2006; Race, 2007). A lecture can also provide students the opportunity to interact with the instructor by asking questions (Brown and Race, 2005). Lecture may be sufficient in promoting cognitive learning at the levels of remembering and understanding but may not be effective in promoting cognitive learning at the higher levels of application, analysis, synthesis, and evaluation (Bligh, 2000; Charlton, 2006). Animal science students who continue on to careers in agriculture need a few specific professional skills such as self-reliance, problem-solving, and decision-making (Wattiaux, 2009). The development of these professional skills could arise from higher-order cognitive learning (i.e., application, analysis, synthesis, and evaluation) in animal science degree

[8] Ferree, L., N. Román-Muñiz, L. Edwards-Callaway, T. Buchan, J. Todd, and C. Cramer. 2022. Assessing the effect of case-based teaching compared with lecture-based teaching on students' knowledge and perceptions in a senior undergraduate dairy cattle management course. Translational Animal Science. Vol 6. Issue 2. https://doi.org/10.1093/tas/txac033

programs to equip animal science students with the necessary skills needed in their future careers (e.g., self-reliance, problem-solving, and decision-making; Wattiaux, 2009). Pedagogical research in healthcare fields suggests that case-based (CB) teaching may be an ideal teaching method for animal science students needing to develop professional skills similar to those of healthcare students (e.g., profession-specific skills, knowledge creation capacity, and theoretical knowledge; Hanson and Sinclair, 2008). Students in healthcare need to be able to solve a problem when presented a case (i.e., treat a patient) much like animal scientists need to be able to solve a problem when presented a case (i.e., investigate the cause of profit loss on a dairy). Given that students in healthcare fields require skills similar to students in animal science such as problem-solving, critical thinking, decision-making, and the ability to apply knowledge to real-world situations (Hanson and Sinclair, 2008; Wattiaux, 2009), we can glean potentially useful pedagogical practices from the healthcare fields to apply to teaching animal science students in higher education.

There is not a universal definition of CB teaching, but it is understood that CB methods are referring to the implementation of active learning strategies such as case studies in addition to facilitated hands-on activities to simulate a learning experience as similar to real-life scenarios as possible (Thistlethwaite et al., 2012). Data regarding pedagogical methods in animal sciences are sparse to nonexistent. Case-based teaching is suggested to enhance students' motivation to learn and results in a deeper level of understanding (Gal et al., 2018). Case-based methods can also optimize learning and performance on both CB and non-CB items when CB methods are used in addition to traditional lectures (Panja et al., 2013). There is an agreement in the existing literature that CB methods result in greater development of profession-specific and problem-solving skills (Hanson and Sinclair, 2008; Panja et al., 2013). The presumed benefits of CB teaching methods should be weighed against the perceived drawbacks (e.g., heavy workload and time commitment) before the implementation in curriculum (Gal et al., 2018). It is important to understand how teaching methods impact the development of students' skills, knowledge, and attitude in the classroom. To our knowledge, there is no research evaluating the efficacy of CB teaching methods in animal sciences in higher education. Case-based teaching could be a powerful tool in animal science classrooms in higher education to enhance students' learning experience. Before implementation, it is necessary to determine if CB teaching positively affects student performance and how students perceive this teaching method. Therefore, the objectives of this study were to determine the effects of CB vs. lecture-based (LB) teaching methods on student performance and to assess student attitude toward CB and LB teaching methods in a senior dairy cattle management course at a land-grant university.

3.2 Materials and methods

Our study utilized existing literature to design and implement a cross-over design study in a senior dairy management course at a land-grant university in the United States consisting of undergraduate and graduate students. This study utilized two content modules (module 1 = "calf health" and module 2 = "lameness") with a washout period of 2 wk in between content modules. Undergraduate and graduate students pursuing a degree in Animal Sciences (n = 25) were randomly assigned, using a random number generator in Microsoft Excel (Microsoft Corp., Redmond, WA), to either CB or LB teaching methods for module 1 ("calf health"). Students then received the opposite teaching method in module 2 ("lameness"). Due to COVID-19 university restrictions, the course was taught in a hybrid format which included prerecorded lectures posted on an online learning management system (Canvas; Instructure, Inc., Salt Lake City, UT) and an optional in-person lab once per week. The lab was also recorded and posted online for students to view.

Institutional review board approval and participant recruitment

This study was approved by the Institutional Review Board (IRB) at Colorado State University (protocol # 1952). A member of the research team not involved with the course or data analysis presented the study participation information to the students in the course via video recording posted on an online learning management system. Informed consent was obtained from students by submitting a signed participant agreement (n = 25) and a 1.5% bonus was offered to students for submitting the signed agreement, regardless of participation status. Consent indicated that students opted to allow the research team to use assignment scores and responses for analysis. The course instructors were blinded to the study participation status of students, and data were deidentified by the same member of the research team that presented the study participation information prior to data analysis. All students, regardless of participation in research, completed the same modules and assignments as part of the coursework.

Course content

Course materials (case studies, lectures, student materials such as notes and handouts, and quizzes) were posted on an online learning management system for students to access during the two course modules, for both CB and LB groups. Modules were designed to require similar effort and time (approximately 3 h) and challenge similar levels of cognitive learning defined using Bloom's Taxonomy (Krathwohl, 2002). The same content and learning objectives were covered for CB and LB groups within a module.

Students, regardless of treatment and module, received module content via an online learning management system on a Monday and had the option to attend a 75-min in-person lab section on Friday. Due to guidelines for COVID-19, students could attend this lab section in person, synchronously via Microsoft Teams (Microsoft Corp., Redmond, WA) or asynchronously via a Microsoft Teams (Microsoft Corp., Redmond, WA) recording posted on an online learning management system. The lecture (LB) or the case study (CB) was presented by the course instructor during the 75-min lab section.

Module 1 ("calf health") focused on bovine respiratory disease (BRD) in dairy calves. The learning objectives in module 1 targeted the following cognitive learning levels: remembering, understanding, evaluating, and analyzing (Krathwohl, 2002); learning objectives were the same for both CB and LB. Case-based teaching materials given on a Monday consisted of a "student materials" document containing written paragraphs of information providing students with the definition of BRD, risk factors for BRD, BRD identification strategies, BRD treatment, management strategies of BRD in dairy calves, links to online reading materials relative to BRD in dairy calves, and the calf health case study containing guiding questions. Students in CB were instructed to read the "student materials" and review the calf health case study prior to the lab section on Friday. The calf health case study included a descriptive scenario that asked students to evaluate management factors associated with BRD (e.g., nutrition, colostrum management, ventilation, weather, and more). The calf health case study included questions that were designed so that students had to actively seek out information (Anderson and Krathwohl, 2001) from the "student materials" to evaluate the management factors described in the scenario and their potential effect on BRD. During the 75-min lab section, a course instructor guided the CB students through the questions in the calf health case study, and students were able to converse with peers and the instructor while answering the calf health case study questions. The materials for the LB group in module 1 ("calf health") consisted of four sets of lecture slides covering the same material the CB group received. The students received access to the lecture slides on Monday via an online learning management system. On Friday, students received 75 min of lecture by the same course instructor and were able to ask questions at any time.

Module 2 ("lameness") focused on lameness in adult dairy cows. The learning objectives in module 2 targeted the following cognitive learning levels: remembering, understanding, and evaluating (Krathwohl, 2002); learning objectives were the same for LB and CB. Case-based teaching materials were given on a Monday and consisted of a "student materials" document containing information in the form of written paragraphs providing students with the definition of lameness, risk factors to lameness, identification of lameness, treatment of lameness, management strategies for lameness, links to online reading materials relative to lameness, and the lameness case study. Students in CB were instructed to read the "student materials" and review the lameness case study prior to the lab section on Friday. The lameness case study included a descriptive scenario asking students to evaluate management factors associated with lameness (e.g., flooring, injury, handling, and nutrition). The lameness case study included questions that were designed so that students had to actively seek out information (Anderson and Krathwohl, 2001) from the "student materials" to evaluate the management factors described in the scenario and their potential effect on lameness. During the 75-mi lab section, a course instructor guided the CB students through the questions in the lameness case study, and students were able to converse with peers and the instructor while answering the lameness case study questions. The materials for the LB group in module 2 ("lameness") consisted of four sets of lecture slides covering the same material the CB group received. The students received access to the lecture slides on Monday via an online learning management system. On Friday, students received 75 min of lecture by the same course instructor and were able to ask questions at any time.

To assess performance, students were asked to take both pre- and post-quizzes (maximum score of 10 points possible) for each module which included a 10-question multiple-choice quiz to assess content knowledge and 3 short-answer questions to assess critical thinking. Students completed the pre-quiz at the beginning of the week before any module content was made available to them. Students completed the post-quiz at the end of the week after module content was presented by a course instructor during lab. The pre- and post-quizzes for the CB and LB groups were identical and administered through the online management system. A course instructor graded all students' assignments with the same rubric; student names were anonymized to avoid bias when grading.

Students were asked to complete an attitude assessment after completing each module. The attitude assessment included eight Likert-scale questions with possible responses of "Strongly Agree," "Agree," "Disagree," or "Strongly Disagree." Two free-response questions were also included in the attitude assessment to allow students to freely share their opinions.

Statistical analysis

Three separate mixed linear regression (PROC MIXED) in SAS v 9.4 (SAS Institute Inc., Cary, NC) models were used to assess the effect of teaching method (CB or LB; predictor) on three different continuous outcomes for student performance: change in short-answer quiz score (post-short answer − pre-short answer), change in multiple-choice quiz score (post-multiple choice − pre-multiple choice), and change in total quiz scores ([post-short answer + post-multiple choice] – [pre-short answer + pre-multiple choice]). All models included student as a random effect and module ("calf health" or "lameness") as a fixed effect. The LSMEANS statement was used to obtain means ± SE. Whether or not a student attended lab in person ("lab attendance") was initially included in each model but was removed due to $P > 0.05$.

Student responses to the Likert-scale questions were collapsed to create "Agree" ("Strongly Agree" and "Agree") and "Disagree" ("Strongly Disagree" and "Disagree") for final analysis. The proportion of students who agreed or disagreed with each Likert-scale statement was calculated. A logistic regression (PROC GLIMMIX) in SAS v 9.4 (SAS Institute Inc., Cary, NC) was used to determine if the teaching method (CB or LB; predictor) affected the proportion of students who agreed with each Likert-scale statement (outcome: agree: yes/no). The logistic regression controlled for module ("calf health" and "lameness") and included student as a random effect.

Thematic analysis of the free-response section of the attitude assessment was conducted as described in Braun and Clarke (2006). Three members of the research team performed an initial evaluation of student free responses to identify recurrent ideas and develop emergent themes. The three initial coders each offered a unique perspective and experience level to the analysis. One coder was the instructor and has both qualitative and quantitative research experience. The second coder was a graduate student blinded to treatment with knowledge of study design. The third coder was an undergraduate student with no connection to the project or course, who provided a fresh, outside perspective. Two of these three members then independently coded student free responses for theme. The original interobserver agreement for thematic analysis was 92%. Interobserver agreement for the thematic analysis was calculated by dividing the number of codes that were coded the same by the two observers by the total number of codes completed. One hundred percent interobserver agreement was achieved through little discussion between the two observers.

3.3 Results

One student did not submit the pre-quiz for either module, so their scores were excluded from quantitative analysis. Twenty-four students were included in the final quantitative analysis, and 25 students were included in the final qualitative and thematic analysis. The raw mean scores of each assignment are presented in Table 5. Means of the change in post- and pre-quiz scores are presented in Table 6.

Table 5. Raw scores (mean ± SD) on course assessments, by module and teaching method (*n* = 24 students)

Module	**Assessment Type**	**CB teaching method**	**LB teaching method**
Calf Health	Pre-quiz	5.65 (±1.04)	6.23 (±1.68)
Calf Health	Post-quiz	7.73 (±1.19)	7.72 (±1.43)
Calf Health	Pre-short answer	2.91 (±1.1)	2.42 (±0.82)
Calf Health	Post-short answer	3.32 (±0.99)	3.46 (±0.85)
Lameness	Pre-quiz	7.92 (±1.55)	8.55 (±1.13)
Lameness	Post-quiz	9.23 (±0.93)	8.45 (±0.93)
Lameness	Pre-short answer	3.10 (±1.23)	2.88 (±1.31)

Lameness	Post-short answer	3.75 (±1.17)	3.91 (±0.99)

Table 6. Least-squares means (±SE) for change in quiz score between CB and LB teaching methods, after controlling for module (*n* = 24 students)

Assessment	**CB teaching methods**	**LB teaching methods**	**P-value**
Change in multiple-choice quiz score	1.7 ± 0.32	0.8 ± 0.33	0.06
Change in short-answer quiz score	0.02 ± 0.4	0.6 ± 0.4	0.1
Change in total quiz score	1.5 ± 0.6	1.2 ± 0.6	0.5

Student performance on quizzes

There was no difference (mean ± SE) between CB and LB for the change in short-answer quiz scores (0.02 ± 0.4 vs. 0.6 ± 0.4; $P = 0.1$), the change in multiple-choice quiz scores (1.7 ± 0.32 vs. 0.8 ± 0.33; $P = 0.06$), or the change in total quiz scores (1.5 ± 0.6 vs. 1.2 ± 0.6, respectively; $P = 0.5$).

Attitude assessments

For the statement "I enjoyed the teaching method used in this module," 68% (17/25) of CB students agreed, compared with 96% (24/25; Table 7) of LB students (*P* = 0.03). For the statement "I wish this teaching method was utilized in more of my classes," 60% (15/25) of CB students agreed, compared with 88% (22/25) of LB students (*P* = 0.04; Table 7). The proportion of students who agreed for the remaining six Likert-scale statements was not different between CB and LB (*P* > 0.17; Table 7).

Table 7. Difference in proportions of students (*n* = 25) who agreed with each survey statement between CB teaching and LB teaching methods (%, (*n*/*n*))

Survey statement	**Agree CB teaching**	**Agree LB teaching**	**P-value**
I felt I learned a lot during this module.	84% (21/25)	96% (24/25)	0.17
I enjoyed the teaching method used in this module.	76% (19/25)	100% (25/25)	0.03
The amount of time I spent on this module was reasonable.	96% (24/25)	88% (22/25)	0.74
I felt the assignments were too demanding.	24% (6/25)	35% (9/25)	0.69
I felt the assignments improved my critical thinking skills.	80% (20/25)	80% (20/25)	1

I felt the assignments improved my problem-solving skills.	80% (20/25)	64% (16/25)	0.19
I felt this module was applicable to the real world and provided practical application of the material.	96% (24/25)	92% (23/25)	0.60
I wish this teaching method was utilized in more of my classes.	60% (15/25)	88% (22/25)	0.04

Themes from attitude assessment free-response

Five themes emerged from the analysis: preference, COVID-19, perceived drawbacks, perceived benefits, and awareness of available course materials. Eighteen total subthemes emerged from the main themes (Table 8). The proportion of times each theme was mentioned by students in CB and LB is presented in Table 9. All student responses included in this manuscript are direct quotes and have not been altered. For example, a student stated "I like the lecture but I also like the case studies. I like learning about it and then applying it to a real-life situation. It just helps me put it all together and apply it.," which was coded as both preference and perceived benefits. The phrase “I like learning about it and then applying it to a real-life situation” conveys the recurring theme of preference for the order in which the course material is presented. The phrase “It just helps me put it all together and apply it” conveys the recurring theme of perceived benefits of the teaching method utilized.

Table 8. Themes and subthemes from thematic analysis of survey attitude assessment free-response answers (*n* = 25 students)

Theme	**Subthemes**
Preference	Combination of teaching methods, sequence of teaching methods, hands-on, professor interaction, organization, consistency, and discussion among peers
Perceived benefits	Applicable to real life, hands-on application for future, critical thinking, self-paced, and retention
Perceived drawbacks	Oversimplified, workload, accessing materials was confusing
COVID-19	In-person, virtual learning challenges
Awareness of available materials	Impossible to access and utilize materials

Table 9. Proportion of times theme was mentioned by students (*n* = 25) in the thematic analysis of survey attitude assessment free-response answers

Theme	Proportion of times mentioned CB (%)	Proportion of times mentioned LB (%)
Preference	80	84
Perceived benefits	44	40
Perceived drawbacks	28	18
COVID-19	12	18
Awareness of available materials	0	0.2
Other	0.2	0.4

The theme preference included responses that indicated a preference for teaching method or teaching practices. Preference emerged in 80% (Table 9) of CB comments and 84% (Table 9) of LB comments. Student responses included a range of preferences including preferring lecture, the order the material is presented by method, and a clear indication of dislike. Within the theme of preference, a subtheme of "order of teaching methods" arose from students directly stating that they prefer to first have information directly explained to them in a lecture before being exposed to a case study that requires them to work through real-life scenarios. Preference for order of teaching methods was also observed in our students who explained that they believe they learn best by having new concepts explained to them directly instead of navigating new content on their own. The subtheme order of teaching methods revealed a consensus that students in our study preferred to be introduced to new material via an instructor-guided lecture rather than CB teaching methods.

Additionally, within the theme of preference, a subtheme of "single teaching method" emerged from students' comments stating preference for either CB or LB teaching methods or a preference for consistency of teaching method. Some students in our study stated that they did not prefer a specific teaching method in a classroom but rather prefer that instructors are consistent with the teaching method used. Several students in our study stated that case studies should not be the sole, or primary, teaching method used but instead a supplement to LB teaching. The majority of students in our study preferred lecture as the primary teaching method justified by the structure associated with lecture. The subtheme of a "single teaching method" is informative that not all students appreciate/enjoy the same teaching methods; in fact, some students feel very strongly one way or another as seen in the comments. Within the theme of preference, we also observed students' preference for utilizing a mixture of teaching methods that would include more interactive discussion and less memorization-based assignments.

The theme of perceived drawbacks included responses that discussed a perceived drawback of the teaching method utilized in the module. Perceived drawbacks were more frequently discussed in regard to CB teaching (28%; Table 9) compared with LB teaching (18%; Table 9). Students in our study disliked the independent nature of CB teaching for fear of confusion and misinformation when not guided through new material by an instructor. Case-based students also discussed being overwhelmed by the amount of reading and time associated with CB teaching in this study. Some students expressed dislike of the redundant nature of lectures and lack of hands-on activities in LB teaching in this study.

The perceived benefits theme included responses that discussed students' perceived benefits of the teaching method utilized in the module. Perceived benefits were more frequently discussed in regard to CB teaching (44%; Table 9) than LB teaching (40%; Table 9). Many students discussed critical thinking, real-life application, and deeper understanding as benefits of CB learning. Within perceived benefits, a subtheme of "real-life application" emerged from several CB students who stated that CB teaching allowed them to easily apply knowledge to real-life scenarios. A few students stated that they believed they learned better using CB teaching methods than LB because applying knowledge acquired in the learning process to a real-life scenario (case study) helped them better understand the material than listening to a lecture and taking an exam. Some students did enjoy the deeper understanding of course material attributed to the independent nature of CB teaching. Many students appreciated the following components of lecture in our study: the ability to rewatch lectures in an online environment at their own pace alongside provided, outlined lecture notes that guide them through the course material. Notably, students appreciated the guiding role of an instructor in the learning process for clear communication of new material.

The awareness of available materials theme included responses that indicated unawareness of course materials. This theme emerged mostly in the LB group from student comments expressing a difficulty in finding course materials on the online learning management system. These students expressed a feeling of frustration in the amount of time spent locating course materials that discouraged them from engaging with materials the longer they spent locating them.

The theme of COVID-19 included student responses that discussed learning challenges associated with COVID-19. Students demonstrated an understanding of the challenges of the pandemic (e.g., online learning, limited face-to-face interactions) and expressed a preference for face-to-face interaction and an understanding attitude toward the accommodations their instructor(s) and university had to make.

3.4 Discussion

The objectives of the present study were to assess the effects of CB compared with LB teaching methods on student performance and attitudes in an animal science course in higher education. Though we did not observe a significant change in assessment scores between CB and LB groups, we obtained valuable feedback through the attitude assessment to inform future teaching practices in a similar environment, mainly that students appreciate case studies but want to receive the information via lecture first and students value interaction with their peers and instructor(s).

Student performance

The results of the present study do not indicate a difference in student performance between CB or LB teaching methods and, therefore, do not provide support for or against either method. Interestingly, we did observe a tendency for CB teaching methods to improve student performance on multiple-choice questions. The observed tendency may be explained by the findings from Panja et al. (2013) and Bi et al. (2019), whereby CB teaching methods improved student performance on CB and non-CB assessments. Case-based teaching methods have been associated with a deeper understanding and higher-level learning of the content compared with LB teaching (Panja et al., 2013; Bi et al., 2019). In a meta-analysis, Bredow et al. (2021) reported a consistent finding in existing research that student performance improved when active learning (e.g., CB) was used in addition to lecture. Future research in higher education in animal sciences should evaluate both student performance and attitudes when CB teaching methods are used as an adjunctive method to lecture. This approach is supported by our results from the thematic analysis that indicated students appreciate case studies after receiving course content via lecture. The theme of perceived benefits, in which students explained that the independent nature of CB teaching led to a greater understanding of content, may help explain the tendency for CB teaching methods to improve student performance on multiple-choice questions in our study. Both Panja et al. (2013) and Bi et al. (2019) had larger sample sizes compared with our study and took place over consecutive years rather than two week-long modules as in our study. Observing results such as in the study of Bi et al. (2019) and Panja et al. (2013) may be possible if we repeated our study with a larger sample size over a longer period of time and were not limited by COVID-19 restrictions (i.e., all students could be in person for instruction). Student performance also may not have been significantly different between CB and LB groups in the current study because the quizzes were given immediately after receiving the information, so the recall of information happened over a short period of time (i.e., a few days vs. a few weeks; Panja et al., 2013 and Bi et al., 2019). Undergraduates in a biochemistry course exposed to CB teaching performed better at the beginning and the end of the semester than their classmates not exposed to CB teaching (Kulak et al., 2017). Kulak et al. (2017) suggest that CB teaching may result in better student performance, and greater knowledge retention, over longer periods than non-CB teaching methods. To better assess the long-lasting impact of CB on student performance in animal sciences, future studies should focus on assessing the effect of CB teaching methods on long-term knowledge retention.

Student Preference

Seventy-six percent of students in our CB group "enjoyed the teaching method used in this module" compared with 100% of LB students. Students' enjoyment of LB teaching methods in our study suggests that students may prefer LB over CB. Sixty percent of students in our CB group "wish this teaching method was utilized in more of my classes" compared with 88% of LB students. These results are, in part, explained by the theme of preference derived from the free responses on the attitude assessment. Preference, specifically the subtheme "order of teaching methods' revealed that students in our study enjoyed having new information delivered to them in an instructor-guided lecture before engaging in CB teaching methods.

Students' preference for LB teaching methods in our study contrasts existing literature in which students reported a higher satisfaction with CB methods than LB methods (Panja et al., 2013; Bi et al., 2019). However, the groups exposed to case studies in Panja et al. (2013) and Bi et al. (2019) both participated in smaller group discussions that were not offered in our study. Additionally, Boström and Hallin (2013) reported that approximately half of teaching and nursing students in their study preferred working with peers. However, the students in our study were limited in their ability to interact with one another while learning the material due to COVID-19 social distancing requirements. The theme of perceived benefits revealed that students in our study desire peer discussion in the learning process, and, therefore, student satisfaction of CB methods could be increased through including small, peer discussion groups. Students in our study did have the chance to interact with a course instructor and peers in the optional in-person lab section at the end of the week, but the expectation at this point was that students had already reviewed and learned the module content. Future studies should assess the effect of peer-to-peer interaction on the efficacy of CB teaching methods.

The attitude assessment provided insights into reasons students did or did not enjoy CB teaching in the present study. Student reasoning for the enjoyment of CB teaching methods was extracted from the thematic analysis in the theme perceived benefits and included self-paced, deeper thinking, and interaction with peers and instructor(s) (Table 8). In contrast, student reasoning for not enjoying CB teaching methods was extracted from the thematic analysis in the theme perceived drawbacks and included self-taught and heavy workload, and did not align with personal learning style (Table 8). The themes perceived benefits and perceived drawbacks explain student preferences for teaching methods observed in the theme of preference. From the thematic analysis, we inferred that the perceived benefits and perceived drawbacks of CB teaching methods indicate students may prefer to receive information first via LB teaching methods, followed by a case study to apply the information presented in the lecture. Our results are similar to Boström and Hallin (2013) who reported three of four nursing and teaching students desired clear instruction in the classroom before beginning a task. Likewise, Gal et al. (2018) reported students feel that the professor is an integral part of the learning process. Like Gal et al. (2018), our theme of perceived benefits suggests that students appreciate the guiding role of a professor in LB teaching and may not want to eliminate the professor from the initial instruction process. Instructors interested in integrating CB methods into courses should consider providing some material via lecture, followed by case studies in which students get to interact with their peers and the instructor.

Eighty percent of CB students in our study agreed “the assignments improved my problem-solving skills” compared with 64% of LB students, but there was no difference between our CB and LB groups’ agreement with the statement “I felt the assignments improved my critical thinking skills.” Similarly, Bi et al. (2019) and Mesthrige et al. (2020) found that students perceive CB teaching methods to be beneficial in improving their problem-solving skills. Our theme perceived benefits provides support for similar conclusions to Bi et al. (2019) and Mesthrige et al. (2020) as students in our study expressed that they valued how CB teaching improved their understanding and memory of material which allowed them to better apply their acquired knowledge to the case study presented.

Based on the attitude assessment results, time and workload were not students' primary concern with the teaching methods (Table 7). Almost all students in CB and LB (96% vs. 100%) agreed "the time I spent on this module was reasonable" (Table 7), which agrees with findings in Gal et al. (2018) of the first-year medical students who thought the workload associated with active learning was reasonable. In contrast, Gal et al. (2018) also reported that the second-year medical students in the study perceived the workload associated with active learning as too demanding because the students felt that they had to work on their own as opposed to in a collaborative effort with their peers. Despite 96% of CB students in the present study agreeing with the Likert-scale statement, "the amount of time I spent on this module was reasonable," we received responses indicating negative concerns about the workload associated with CB teaching methods such as time to complete task, associated point value with task, and difficulty navigating content, which were captured in the themes perceived drawbacks and awareness of available materials, respectively.

Lastly, a unique characteristic of our study population is that our study consisted of the third- and fourth-year undergraduates and the first-year graduate students in animal sciences who may not have been previously exposed to CB teaching. Gal et al. (2018) evaluated the differences in student preference for active learning methods in the first- and second-year medical students and found a temporal bias. The first-year students in Gal et al. (2018) had a more positive rating of participatory methodologies (e.g., CB teaching, case studies, and group discussion) compared with the second-year students, suggesting that results in the present study could be influenced by the inclusion of students who were in the later years of their academic career. The medical field utilizes case studies to prepare students to problem-solve when presented with a patient in the field (Gal et al., 2018), much like animal science students may need to problem-solve when presented with a problem in the field (Wattiaux, 2009). Future research should evaluate the effect of previous exposure to CB teaching methods on student performance and attitude toward CB teaching methods compared with LB teaching methods.

Strengths and Limitations

Our study took place amidst the COVID-19 pandemic during which students were quickly forced to transition to an online or hybrid (partially online and partially in person) format that added a layer of complexity to their classroom experience and, in some cases, limited student access to their usual, in-person learning. Students in the present study may have faced challenges outside of the classroom, including unemployment, loss of social contact, poor internet connection, and access to technology and materials (Aristovnik et al., 2020), that may have influenced their performance in our study. Students in the present study acknowledged challenges associated with learning during COVID-19 such as the lack of face-to-face instruction, the lack of peer interaction through discussion-based assignments, and difficulty engaging with the material through online lecture videos. Future instructors in similar conditions as described in our study (i.e., online or hybrid environment) should consider incorporating pedagogical practices that satisfy student desire for live interaction between the students and instructor(s) to compensate for the lack of face-to-face class meetings.

Additionally, our sample size was relatively small because our study population was dependent on the students who enrolled in the senior-level dairy management course in the semester the study took place, and, as such, we did not recruit participants from outside the course. A larger sample size could have potentially resulted in a statistically significant change in students' performance between CB and LB teaching methods. Future studies should consider larger sample sizes, which could be achieved by including multiple animal science courses and conducting the study over multiple semesters.

3.5 Conclusions

The effect of CB and LB teaching methods on student performance was not different in the present study, but student insight received through the attitude assessment provided valuable information that can inform instruction methods in animal sciences in higher education. Overall, students in our study did appreciate CB teaching methods for the discussion and problem-solving aspects but preferred to be presented with the course content in the form of a lecture before engaging in a case study. Students indicated that they appreciate the guidance of an instructor through classroom materials and like to be challenged to apply the knowledge acquired in the classroom to real-life scenarios (e.g., case studies). The COVID-19 pandemic added a unique element to our study and should be considered for its influence on student performance, equity, and well-being. Student comments from our study suggest prioritizing the connection between classroom and real-life application, which can be achieved through introductory lectures and subsequent case studies.

3.6 Thesis conclusions

Both Project 1 and Project 2 investigated topics that have not been well characterized previously in literature and provide baselines for future projects. Respiratory disease has been one of the leading causes of morbidity and mortality in preweaned dairy calves over the last 20 years and likely will continue to be unless effective treatment methods are established. The effect of NSAID group was not associated with performance or health in Project 2. However, Project 2 laid a foundation for investigating oral meloxicam as an ancillary treatment to an antibiotic for respiratory disease in preweaned calves. Future studies can alter the study design or methods by investigating the effects of multiple doses of oral meloxicam or basing measurements around the half-life of meloxicam to observe peak effects. Teaching methods have been well studied throughout the medical field, but have not been widely investigated in agricultural classrooms in higher education. Our study provided the first data on teaching methods utilized in an undergraduate and graduate-level dairy management course. Although we did not observe an effect of teaching method on student attitude or performance in Project 2, we gained insight on student's preferred teaching methods that can be used to design future studies to hone in on implementation of the preferences and utilize a larger sample size. Overall, both projects contributed to their fields of research and provide methods to be improved upon to further characterize the use of oral meloxicam as ancillary treatment for respiratory disease in preweaned calves and effective teaching methods in animal science programs.

REFERENCES

Chapter 1

Ackermann, M.R., R. Derscheid, and J.A. 2010. Roth. Innate immunology of bovine respiratory disease. Vet Clin North Am Food Anim Pract. 26(2):215-28. doi:0.1016/j.cvfa.2010.03.001.

Allen, K.A., J.F. Coetzee, L.N. Edwards-Callaway, H. Glynn, J. Dockweiler, B. KuKanich, H. Lin, C. Wang, E. Fraccaro, M. Jones, and L. Bergamasco. 2013. The effect of timing of oral meloxicam administration on physiological responses in calves after cautery dehorning with local anesthesia. J Dairy Sci. 96(8):5194-205. doi:10.3168/jds.2012-6251.

Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA). 1994. U.S. Food and Drug Administration website. Available at http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/AnimalMedicinalDrugUseClarificationActAMDUCAof1994/default.htm

Apley, M. 2009. Antimicrobials and BRD. Anim Health Res Rev. 10:159-161

Bach, A. 2011. Associations between several aspects of heifer development and dairy cow survivability to second lactation. J Dairy Sci. 94(2):1052-1057.

Bednarek, D., B. Zdzisińska, M. Kondracki, W. Rzeski, R. Paduch, and M. Kandefer-Szerszeń. 2003. A comparative study of the effects of meloxicam and flunixin meglumine (NSAIDs) as adjunctive therapy on interferon and tumor necrosis factor production in calves suffering from enzootic bronchopneumonia. Polish journal of veterinary sciences. 6(2):109-115.

Berkowitz, R.D., R.J. Mack, and S.W. McCallum. 2021. Meloxicam for intravenous use: review of its clinical efficacy and safety for management of postoperative pain. Pain Management. 11(3):249-258.

Boyd, M., K. Clezy, R. Lindley, and R. Pearce. 2006. Pandemic influenza: clinical issues. Med. J. 185(S10):S44–S47. doi: 10.5694/j.1326-5377.2006.tb00706.x

Buczinski, S., G. Forté, and A.M. Bélanger. 2013. Ultrasonographic assessment of the thorax as a fast technique to assess pulmonary lesions in dairy calves with bovine respiratory disease. J Dairy Sci. 96(7):4523-4528.

Caswell, J.L. 2013. Failure of Respiratory Defenses in the Pathogenesis of Bacterial Pneumonia of Cattle. Veterinary Pathology. 51:393-409.https://doi.org/10.1177/030098581350282

Closs, G. Jr., and C. Dechow. 2017. The effect of calf-hood pneumonia on heifer survival and subsequent performance. Livest. Sci. 205:5–9. https:/ / doi.org/10 .1016/ j.livsci.2017.09 .004.

Coetzee, J.F., B. KuKanich, R. Mosher, P.S. Allen. 2009. Pharmacokinetics of intravenous and oral meloxicam in ruminant calves. Vet Ther. 10 (4): E1-E8.

Cramer, M.C. and T.L. Ollivett. 2019. Growth of preweaned, group-housed dairy calves diagnosed with respiratory disease using clinical respiratory scoring and thoracic ultrasound—A cohort study. Journal of Dairy Science. Volume 102, Issue 5. Pages 4322-4331. ISSN 0022-0302.

Cuevas-Gómez, I., M. McGee, J.M. Sánchez, J. E. O'Riordan, N. Byrne, T. McDaneld, and B. Earley. 2021. Association between clinical respiratory signs, lung lesions detected by thoracic ultrasonography and growth performance in pre-weaned dairy calves. Irish Veterinary Journal, 74(1):1-9.

Curtis, G., C. McGregor Argo, D. Jones, and D. Grove-White. 2018. The impact of early life nutrition and housing on growth and reproduction in dairy cattle. PloS one. 13(2).

Dantzer, R. 2004. Cytokine-induced sickness behaviour: a neuroimmune response to activation of innate immunity. Eur J Pharmacol. 500(1-3):399-411. doi: 10.1016/j.ejphar.2004.07.040. PMID: 15464048.

Davies, N.M. and N.M. Skjodt. 1999. Clinical Pharmacokintics of Meloxicam: A cyclo-oxygenase-2 preferential nonsteroidal anti-inflammatory drug. Clin. Pharmacokinet. 36:115–126.

Day, R.O. and G.G. Graham. 2004. The vascular effects of COX-2 selective inhibitors. Aust Prescr. 27:142-5. https://doi.org/10.18773/austprescr.2004.119

Delabouglise, A., A. James, J.F. Valarcher, S. Hagglünd, D. Raboisson, and J. Rushton. 2017. Linking disease epidemiology and livestock productivity: The case of bovine respiratory disease in France. PLoS One, 12(12), e0189090.

Donovan, G. A., I.R. Dohoo, D.M. Montgomery, and F.L. Bennett. (1998). Calf and disease factors affecting growth in female Holstein calves in Florida, USA. Preventive veterinary medicine, 33(1-4), 1-10.

Dubrovsky, S.A., A.L. Van Eenennaam, B.M. Karle, P.V. Rossitto, T.W. Lehenbauer, S.S. Aly. 2019. Epidemiology of bovine respiratory disease (BRD) in preweaned calves on

California dairies: The BRD 10K study. J Dairy Sci. 2019a. 102(8):7306-7319. doi:10.3168/jds.2018-14774.

Dubrovsky, S. A., A.L. Van Eenennaam, B.M. Karle, P.V. Rossitto, T.W. Lehenbauer, and S.S. Aly. 2019b. Bovine respiratory disease (BRD) cause-specific and overall mortality in preweaned calves on California dairies: The BRD 10K study. J Dairy Sci. 102(8):7320-7328.

Dubrovsky, S. A., A.L. Van Eenennaam, S.S. Aly, B.M. Karle, P.V. Rossitto, M.W. Overton, and J.G. Fadel. 2020. Preweaning cost of bovine respiratory disease (BRD) and cost-benefit of implementation of preventative measures in calves on California dairies: The BRD 10K study. J Dairy Sci. 103(2):1583-1597.

Dunn, T.R., T.L. Ollivett, D.L. Renaud, K.E. Leslie, S.J. LeBlanc, T.F. Duffield, and D.F. Kelton. 2018. The effect of lung consolidation as determined by ultrasonography on first-lactation milk production in Holstein dairy calves. J Dairy Sci. 101:5404–5410. doi: 10.3168/jds.2017-13870.

Ferreira, S.H. 1983. Prostaglandins: peripheral and central analgesia. J.L. Bonica (Ed.). Advances in Pain Research and Therapy. Raven Press.

Francoz, D., S. Buczinski, and M. Apley. 2012. "Evidence related to the use of ancillary drugs in bovine respiratory disease (anti-inflammatory and others): are they justified or not?." Veterinary Clinics: Food Animal Practice 28.1: 23-38.

Gulliksen S.M., E. Jor, K.I. Lie, T. Løken, J. Akerstedt, and O. Østerås. 2009. Respiratory infections in Norwegian dairy calves. J Dairy Sci. 92(10):5139-46. doi: 10.3168/jds.2009-2224.

Guzel, M., M.C. Karakurum, R. Durgut, and N. Mamak. 2010. Clinical efficacy of diclofenac sodium and flunixin meglumine as adjuncts to antibacterial treatment of respiratory disease of calves. Australian veterinary journal. 88(6):236-239. Doi:10.1111/j.1751-0813.2010.00575.x.

Hart, B.L. 1998. Biological basis of the behavior of sick animals. Neurosci Biobehav Rev. 12:123–137.

Heinrich, A., T.F. Duffield, K.D. Lissemore, and S.T. Millman. 2010. The effect of meloxicam on behavior and pain sensitivity of dairy calves following cautery dehorning with a local anesthetic J. Dairy Sci., 93. pp. 2450-2457.

Heins, B. D., D.V. Nydam, A.R. Woolums, R.D. Berghaus, and M.W. Overton. 2014. Comparative efficacy of enrofloxacin and tulathromycin for treatment of preweaning respiratory disease in dairy heifers. J Dairy Sci. 97(1):372-382.

Hudson, C., H. Whay, and J. Huxley. 2008. Recognition and management of pain in cattle. In Practice. 30(3):126-134.

Jourquin, S., J. Bokma, L. De Cremer, K. van Leenen, N. Vereecke, and B. Pardon. 2022. Randomized field trial comparing the efficacy of florfenicol and oxytetracycline in a natural outbreak of calf pneumonia using lung reaeration as a cure criterion. J Vet Intern Med. 36(2): 820- 828. doi:10.1111/jvim.16348

Karle, B.M., G.U. Maier, W.J. Love, S.A. Dubrovsky, D.R. Williams, R.J. Anderson, A.L. Van Eenennaam, T.W. Lehenbauer, and S.S. Aly. 2019. Regional management practices and prevalence of bovine respiratory disease in California's preweaned dairy calves. J Dairy Sci.102(8):7583-7596. https://doi.org/10.3168/jds.2018-14775.

Koster, J., J-K. Tena, M.R. Stegemann. 2021. Treatment of bovine respiratory disease with a single administration of tulathromycin and ketoprofen. Vet Rec. https://doi.org/10.1002/vetr.834

Krpálková, L., V.E. Cabrera, J. Kvapilík, J. Burdych, and P. Crump. 2014. Associations between age at first calving, rearing average daily weight gain, herd milk yield and dairy herd production, reproduction, and profitability. Journal of Dairy Science. 97(10):6573-6582. https://doi.org/10.3168/jds.2013-7497.

Lago, A., S.M. McGuirk, T.B. Bennett, N.B. Cook, and K.V. Nordlund. 2006. Calf respiratory disease and pen microenvironments in naturally ventilated calf barns in winter. J Dairy Sci. 89(10):4014-25. doi: 10.3168/jds.S0022-0302(06)72445-6.

Lees, P. 2009. Analgesic, anti-inflammatory, antipyretic drugs. Veterinary pharmacology and therapeutics. 9th edition. Edited by: Riviere JM, Papich MG. Ames, IA, USA: Wiley-Blackwell; 457-492.

Mahendran, S. A. 2020. Use of fever detection in combination with thoracic ultrasonography to identify respiratory disease, and compare treatments of antimicrobials and NSAID: a randomised study in dairy calves. Veterinary record open. 7(1). e000415.

Mahendran, S.A., R. Booth, N.J. Bell, M. Burge. 2017. Randomised positive control trial of NSAID and antimicrobial treatment for calf fever caused by pneumonia. Vet Rec. 181(2):45. doi: 10.1136/vr.104057.

Martin, M.S., M.D. Kleinhenz, B.J. White, B.T. Johnson, S.R. Montgomery, A.K. Curtis, M.M. Weeder, D.A. Blasi, K.M. Almes, R.G. Amachawadi, H.M. Salih, M.D. Miesner, A.K. Baysinger, J.S. Nickell, and J.F. Coetzee. 2022. Assessment of pain associated with bovine respiratory disease and its mitigation with flunixin meglumine in cattle with induced bacterial pneumonia. J Anim Sci. 100(2):skab373. doi: 10.1093/jas/skab373.

McGill, J.L., and R.E. Sacco. 2020. The Immunology of Bovine Respiratory Disease: Recent Advancements. Vet Clin North Am Food Anim Pract. 36(2):333-348. doi: 10.1016/j.cvfa.2020.03.002.

McGuirk, S.M. 2008. Disease management of dairy calves and heifers. Vet Clin North Am Food Anim Pract. 24(1):139-53. doi: 10.1016/j.cvfa.2007.10.003.

McGuirk, S.M. and S.F. Peek. 2014. Timely diagnosis of dairy calf respiratory disease using a standardized scoring system. Anim Health Res Rev. 15(2):145-7. doi: 10.1017/S1466252314000267.

Medrano-Galarza, C., S.J. LeBlanc, A. Jones-Bitton, T.J. DeVries, J. Rushen, A.M. de Passillé, and D.B. Haley. 2018. Associations between management practices and within-pen prevalence of calf diarrhea and respiratory disease on dairy farms using automated milk feeders. J Dairy Sci. 101(3):2293-2308.

Molony, V. 1996. Comments on Anand and Craig. Pain. 67:3–6.

Mosher, R.A., J.F. Coetzee, C.A. Cull, R. Gehring, and B. KuKanich. 2012. Pharmacokinetics of oral meloxicam in ruminant and preruminant calves. J. Vet. Pharmacol. Ther. 35:373-381.

Ollivett, T. L., J.L. Caswell, D.V. Nydam, T. Duffield, K.E. Leslie, J. Hewson, and D. Kelton. 2015. Thoracic Ultrasonography and Bronchoalveolar Lavage Fluid Analysis in Holstein Calves with Subclinical Lung Lesions. Journal of Veterinary Internal Medicine. 29(6):1728-1734.

Ollivett, T.L., and S. Buczinski. 2016. On-Farm Use of Ultrasonography for Bovine Respiratory Disease. Vet Clin North Am Food Anim Pract. 32(1):19-35. doi: 10.1016/j.cvfa.2015.09.001.

Olson, M. E., B. Ralston, L. Burwash, H. Matheson-Bird, and N.D. Allan. 2016. Efficacy of oral meloxicam suspension for prevention of pain and inflammation following band and surgical castration in calves. BMC Veterinary Research. 12(1): 1-11.

Poulsen K.P. and S.M. McGuirk. 2009. Respiratory disease of the bovine neonate. Vet Clin North Am Food Anim Pract. 25(1):121-37, vi-vii. doi: 10.1016/j.cvfa.2008.10.007.

Rabeling, B., J. Rehage, D. Döpfer, and H. Scholz. 1998. Ultrasonographic findings in calves with respiratory disease. Veterinary record. 143(17):468-471.

Rossini, K. L. 2004. Effects of calfhood respiratory and digestive disease on calfhood morbidity and first lactation production and survival rates (Doctoral dissertation, Virginia Tech).

Sawant, A.A., L.M. Sordillo, and B.M. Jayarao. 2005 A Survey on Antibiotic Usage in Dairy Herds in Pennsylvania. J Dairy Sci. 88(8):2991-2999. https://doi.org/10.3168/jds.S0022-0302(05)72979-9.

Schaffer, A. P., R.L. Larson, N. Cernicchiaro, G.A. Hanzlicek, S.J. Bartle, and D.U. Thomson. 2016. The association between calfhood bovine respiratory disease complex and subsequent departure from the herd, milk production, and reproduction in dairy cattle. Journal of the American Veterinary Medical Association. 248(10):1157-1164

Scheftel, J. M., B.L. Elchos, B. Cherry, E.E. DeBess, S.G. Hopkins, J.F. Levine, and C.A. Silvia. 2010. Compendium of veterinary standard precautions for zoonotic disease prevention in veterinary personnel: National Association of State Public Health Veterinarians Veterinary Infection Control Committee. Journal of the American Veterinary Medical Association. 237(12): 1403-1422.

Sivula, N.J., T.R Ames, W.E Marsh, and R.E Werdin, 1996. Descriptive epidemiology of morbidity and mortality in Minnesota dairy heifer calves, Preventive Veterinary Medicine. 27(3–4):155-171. https://doi.org/10.1016/0167-5877(95)01000-9.

Stanton, A.L., D.F. Kelton, S.J. LeBlanc, J. Wormuth, and K.E. Leslie. 2012 The effect of respiratory disease and a preventative antibiotic treatment on growth, survival, age at first calving, and milk production of dairy heifers. J Dairy Sci. 95(9):4950-4960. doi: 10.3168/jds.2011-5067. PMID: 22916899.

Svensson, C. and J. Hultgren. 2008. Associations between housing, management, and morbidity during rearing and subsequent first-lactation milk production of dairy cows in southwest Sweden. J Dairy Sci. 91(4):1510-1518.

Taylor, J.D., R.W. Fulton, T.W. Lehenbauer, D.L. Step, and A.W. Confer. 2010. The epidemiology of bovine respiratory disease: What is the evidence for predisposing factors? Can Vet J. 51(10):1095-102.

Teixeira, A. G. V., J.A.A. McArt, and R.C. Bicalho. 2017. Thoracic ultrasound assessment of lung consolidation at weaning in Holstein dairy heifers: Reproductive performance and survival. J Dairy Sci. 100(4):2985-2991.

Timsit, E, N. Tison, C.W. Booker, and S. Buczinski. 2019. Association of lung lesions measured by thoracic ultrasonography at first diagnosis of bronchopneumonia with relapse rate and growth performance in feedlot cattle. J Vet Intern Med. 33:1540– 1546. https://doi.org/10.1111/jvim.15483

Toaff-Rosenstein, R. L., L. J. Gershwin, A.J. Zanella, and C.B. Tucker. 2016. The sickness response in steers with induced bovine respiratory disease before and after treatment with a non-steroidal anti-inflammatory drug. Applied Animal Behaviour Science. 181:49-62. https://doi.org/10.1016/j.applanim.2016.05.016.

Urie, N.J., J.E. Lombard, C.B. Shivley, C.A. Kopral, A.E. Adams, T.J. Earleywine, J.D. Olson, and F.B. Garry. 2018. Preweaned heifer management on US dairy operations: Part V. Factors associated with morbidity and mortality in preweaned dairy heifer calves. J Dairy Sci. 101(10):9229-9244. https://doi.org/10.3168/jds.2017-14019.

USDA. 1994. Dairy Heifer Morbidity, Mortality, and Health Management Focusing on Preweaned Heifers, April 1991-July 1992. National Animal Health Monitoring System (NAHMS) – National Dairy Heifer Project (NDHP).

USDA. 2002. Part II: Changes in the United States Dairy Industry, 1991-2002. USDA:APHIS:VS,CEAH, National Animal Health Monitoring System, Fort Collins, CO #N388.0603.

USDA. 2007. Part V: Changes in dairy cattle health and management practices in the United States, 1996–2007. Fort Collins (CO): USDA: APHIS:VS, CEAH; 2009 #519.0709.

USDA. 2012. Dairy Heifer Raiser, 2011. USDA–APHIS–VS, CEAH, National Animal Health Monitoring System (NAHMS), Fort Collins, CO #613.1012

USDA. 2018. Dairy 2014, 'Health and Management Practices on U.S. Dairy Operations, 2014'.

USDA-APHIS-VS-CEAH-NAHMS, Fort Collins, CO, 80526-8117.

Viñuela-Fernández, I., E. Jones, E.M. Welsh, and S.M. Fleetwood-Walker. 2007. Pain mechanisms and their implication for the management of pain in farm and companion animals. The Veterinary Journal. 174(2):227-239.

Virtala, A. M., G.D. Mechor, Y.T. Gröhn, and H.N. Erb. 1996. The effect of calfhood diseases on growth of female dairy calves during the first 3 months of life in New York State. J Dairy Sci. 79(6):1040-1049.

Webster, A.J. 2001. Farm animal welfare: the five freedoms and the free market. Vet J. 161(3):229-37. doi: 10.1053/tvjl.2000.0563.

Chapter 2

Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA). 1994. U.S. Food and Drug Administration website. Available at http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/AnimalMedicinalDrugUseClarificationActAMDUCAof1994/default.htm

Bednarek, D., B. Zdzisińska, M. Kondracki, and M. Kandefer-Szerszeń. 2003. Effect of steroidal and non-steroidal anti-inflammatory drugs in combination with long-acting oxytetracycline on non-specific immunity of calves suffering from enzootic bronchopneumonia. Veterinary Microbiology. 96(1):53-67. https://doi.org/10.1016/S0378-1135(03)00203-7.

Binversie, E.S., P.L. Ruegg, D.K. Combs, and T.L. Ollivett. 2020. Randomized clinical trial to assess the effect of antibiotic therapy on health and growth of preweaned dairy calves diagnosed with respiratory disease using respiratory scoring and lung ultrasound. J of Dairy Sci.103(12):11723-11735. https://doi.org/10.3168/jds.2019-18044.

Cramer, M.C. and T.L. Ollivett. 2019. Growth of preweaned, group-housed dairy calves diagnosed with respiratory disease using clinical respiratory scoring and thoracic ultrasound—A cohort study. J Dairy Sci.102(5): 4322-4331.

M.C. Cramer, K.L. Proudfoot, and T.L. Ollivett. 2019. Short communication: Behavioral attitude scores associated with bovine respiratory disease identified using calf lung ultrasound and clinical respiratory scoring. J Dairy Sci. 102(7):6540-6544. https://doi.org/10.3168/jds.2018-15550.

Coetzee, J.F., B. KuKanich, R. Mosher, and P.S. Allen. 2009. Pharmacokinetics of intravenous and oral meloxicam in ruminant calves. Vet Ther. 10(4): E1-E8.

Coetzee J.F., L.N. Edwards, R.A. Mosher, N.M. Bello, A.M. O'Connor, B. Wang, B. Kukanich, and D.A. Blasi. 2012. Effect of oral meloxicam on health and performance of beef steers relative to bulls castrated on arrival at the feedlot. J Anim Sci.90(3):1026-39. doi: 10.2527/jas.2011-4068.

Davis, H. P., W. W. Swen, and W. R. Harvey. 1961. Relation of heart girth to weight in Holstein and Jerseys. Nebraska Agric. Exp. Stn. Res. Bull. 194, Univ. Nebraska, Lincoln.

Dubrovsky, S.A., A.L. Van Eenennaam, S.S. Aly, B.M. Karle, Paul V. Rossitto, M.W. Overton, T.W. Lehenbauer, and J.G. Fadel. 2020. Preweaning cost of bovine respiratory disease (BRD) and cost-benefit of implementation of preventative measures in calves on California dairies: The BRD 10K study. J Dairy Sci. 103(2):1583-1597. https://doi.org/10.3168/jds.2018-15501.

Dunn, T.R., T.L. Ollivett, D.L. Renaud, K.E. Leslie, S.J. LeBlanc, T.F. Duffield, and D.F. Kelton. 2018. The effect of lung consolidation as determined by ultrasonography on first-lactation milk production in Holstein dairy calves. J Dairy Sci. 101:5404–5410. doi: 10.3168/jds.2017-13870.

Friton, G.M., C. Cajal, and R. Ramirez-Romero. 2005. Long-term effects of meloxicam in the treatment of respiratory disease in fattening cattle. Veterinary Record. 156. 809-81.

Guzel, M., M.C. Karakurum, R. Durgut, and N. Mamak. 2010. Clinical efficacy of diclofenac sodium and flunixin meglumine asadjuncts to antibacterial treatment of respiratory disease of calves. Australian Veterinary Journal. 88:236–239. Doi:10.1111/j.1751-0813.2010.00575.x.

Heinrich, A., T.F. Duffield, K.D. Lissemore, and S.T. Millman. 2010. The effect of meloxicam on behavior and pain sensitivity of dairy calves following cautery dehorning with a local anesthetic J. Dairy Sci. 93:2450-2457.

Lees, P. 2009. Analgesic, anti-inflammatory, antipyretic drugs. Veterinary pharmacology and therapeutics. 9th edition. Edited by: Riviere JM, Papich MG. Ames, IA, USA: Wiley-Blackwell; 457-492.

Lockwood, P.W., J.C. Johnson, and T.L. Katz. 2003. Clinical efficacy of flunixin, carprofen and ketoprofen as adjuncts to the antibacterial treatment of bovine respiratory disease. Vet. Rec. 152:392-394.

Mahendran, S. A. 2020. Use of fever detection in combination with thoracic ultrasonography to identify respiratory disease, and compare treatments of antimicrobials and NSAID: a randomised study in dairy calves. Veterinary record open. 7(1):e000415.

Martin, M.S., M.D. Kleinhenz, B.J. White, B.T. Johnson, S.R. Montgomery, A.K. Curtis, M.M. Weeder, D.A. Blasi, K.M. Almes, R.G. Amachawadi, H.M. Salih, M.D. Miesner, A.K. Baysinger, J.S. Nickell, and J.F. Coetzee. 2022. Assessment of pain associated with bovine respiratory disease and its mitigation with flunixin meglumine in cattle with induced bacterial pneumonia. J Anim Sci. 100(2):skab373. doi: 10.1093/jas/skab373.

McGill, J.L., and S.E. Sacco. 2020. The Immunology of Bovine Respiratory Disease: Recent Advancements. Vet Clin North Am Food Anim Pract. 36(2):333-348. doi: 10.1016/j.cvfa.2020.03.002.

McGuirk, S.M. 2008. Disease management of dairy calves and heifers. Vet Clin North Am Food Anim Pract. 24(1):139-53. doi: 10.1016/j.cvfa.2007.10.003. PMID: 18299036.

McGuirk, S.M., and S. F. Peek. 2014. Timely diagnosis of dairy calf respiratory disease using a standardized scoring system. Anim Health Res Rev. 15(2):145-7. doi: 10.1017/S1466252314000267.

Mintline, E.M., M. Stewart, A.R. Rogers, N.R. Cox, G.A. Verkerk, J.M. Stookey, J.R. Webster, and C.B. Tucker. 2013. Play behavior as an indicator of animal welfare: Disbudding in dairy calves. Appl. Anim. Behav. Sci.144:22–30. doi: 10.1016/j.applanim.2012.12.008.

Mosher, R.A., J.F. Coetzee, C.A. Cull, R. Gehring, and B. KuKanich. 2012. Pharmacokinetics of oral meloxicam in ruminant and preruminant calves. J. Vet. Pharmacol. Ther. 35:373-381.

National Animal Health Monitoring System (NAHMS). USDA. 2002. Part II: Changes in the United States Dairy Industry, 1991-2002. USDA:APHIS:VS,CEAH, National Animal Health Monitoring System, Fort Collins, CO #N388.0603.

National Animal Health Monitoring System (NAHMS). USDA. 2007. Part V: Changes in dairy cattle health and management practices in the United States, 1996–2007. Fort Collins (CO): USDA: APHIS:VS, CEAH; 2009 #519.0709.

Ollivett, T.L., D.V. Nydam, T.C. Linden, D.D. Bowman, and M.E. Van Amburgh. 2012. Effect of nutritional plane on health and performance in dairy calves after experimental infection with Cryptosporidium parvum. J. Am. Vet. Med. Assoc. 241:1514-1520.

Ollivett, T.L., and S. Buczinski. 2016. On-Farm Use of Ultrasonography for Bovine Respiratory Disease. Vet Clin North Am Food Anim Pract. 32(1):19-35. doi: 10.1016/j.cvfa.2015.09.001.

Olson, M. E., B. Ralston, L. Burwash, H. Matheson-Bird, and N.D. Allan. 2016. Efficacy of oral meloxicam suspension for prevention of pain and inflammation following band and surgical castration in calves. BMC Veterinary Research. 12(1): 1-11.

Reedman, C. N., T. F. Duffield, T. J. DeVries, K. D. Lissemore, S. J.J. Adcock, C.B. Tucker, S.D. Parsons, and B. Winder. 2022. Effect of plane of nutrition and analgesic drug treatment on wound healing and pain following cautery disbudding in preweaning dairy calves. J Dairy Sci. 105(7):6220-6239. https://doi.org/10.3168/jds.2021-21552.

Rosadiuk, J.P., T.C. Bruinjé, F. Moslemipur, A.J. Fischer-Tlustos, D.L. Renaud, D.J. Ambrose, and M.A. Steele. 2021. Differing planes of pre- and postweaning phase nutrition in Holstein heifers: I. Effects on feed intake, growth efficiency, and metabolic and development indicators. J Dairy Sci. 104(1):1136-1152. https://doi.org/10.3168/jds.2020-18809.

USDA. 2018. Dairy 2014, 'Health and Management Practices on U.S. Dairy Operations, 2014'.

USDA-APHIS-VS-CEAH-NAHMS, Fort Collins, CO, 80526-8117.

Chapter 3

Anderson, L. W. and D. R. Krathwohl. 2001. A taxonomy for learning, teaching, and assessing: a revision of Bloom's taxonomy of educational objectives. Longman, New York, NY.

Aristovnik, A., D. Keržič, D. Ravšelj, N. Tomaževič, and L. Umek. 2020. Impacts of the COVID-19 pandemic on life of higher education students: a global perspective. Sustainability 12:8438. doi:10.3390/su12208438

Bi, M., Z. Zhao, J. Yang, and Y. Wang. 2019. Comparison of case-based learning and traditional method in teaching postgraduate students of medical oncology. Med. Teach. 41:1124–1128. doi:10.1080/0142159X.2019.1617414

Bligh, D. 2000. What's the use of lectures? 5th ed. Jossey-Bass, San Francisco, CA.

Boström, L., and K. Hallin. 2013. Learning style differences between nursing and teaching students in Sweden: a comparative study. Int. J. High. Educ. 2:33–34. doi:10.5430/ijhe.v2n1p22

Braun, V., and V. Clarke. 2006. Using thematic analysis in psychology. Qual. Res. Psychol. 3:77. doi:10.1191/1478088706qp063oa

Bredow, C. A., P. V. Roehling, A. J. Knorp, and A. M. Sweet. 2021. To flip or not to flip? A meta-analysis of the efficacy of flipped learning in higher education. Rev. Educ. Res. 91:878–918. doi:10.3102%2F00346543211019122

Brown, S., and P. Race. 2005. Lecturing: a practical guide. Routledge, Sterling, VA.

Charlton, B. G. 2006. Lectures are such an effective teaching method because they exploit evolved human psychology to improve learning. Med. Hypotheses. 67:1261–1265. doi:10.1016/j.mehy.2006.08.001

Gal, B., M. Rubio, E. Iglesias, and P. González. 2018. Evaluation of participatory teaching methods in undergraduate medical students' learning along the first academic courses. PLoS One.13:e01901731. doi:10.1371/journal.pone.0190173

Hanson, J. M., and K. E. Sinclair. 2008. Social constructivist teaching methods in Australian universities – reported uptake and perceived learning effects: a survey of lecturers. High. Educ. Res. Dev. 27:169–186. doi:10.1080/07294360802183754

Krathwohl, D. R. 2002. A revision of bloom's taxonomy: an overview. Theory Pract. 41:212–218. doi:10.1207/s15430421tip4104_2

Kulak, V., G. Newton, and R. Sharma. 2017. Does the use of case-based learning impact the retention of key concepts in undergraduate biochemistry? Int. J. High. Educ. 6:110–120. doi:10.5430/ijhe.v6n2p110

Mesthrige, J., P. T. I. Lam, Y. Chiang, and T. I. Samarasinghalage. 2020. Effectiveness of case-based learning: views of construction and real estate students. Int. J. Constr. Educ. Res. 17:318–332. doi:10.1080/15578771.2020.1758254

Panja, S., K. Bhowmick, and M. Sadhu. 2013. Efficacy of case-based learning as an adjunct to traditional teaching learning methods in physiology. South-East Asian J. Med. Educ. 7:31–37. doi:10.4038/seajme.v7i1.147

Race, P. 2007. The lecturer's toolkit: a practical guide to assessment, learning and teaching. 3rd ed. Routledge, New York, NY.

Roehl, A., S. L. Reddy, and G. J. Shannon. 2013. The flipped class-room: an opportunity to engage millennial students through active-learning strategies. J. Fam. Consum. Sci. 105:44–49. doi:10.14307/JFCS105.2.12

Thistlethwaite, J. E., D. Davies, S. Ekeocha, J. M. Kidd, C. MacDougall, P. Matthews, J. Purkis, and D. Clay. 2012. The effectiveness of case-based learning in health professional education. A BEME systematic review: BEME guide no. 23. Med. Teach. 34:e421–e444. doi:10.3109/0142159X.2012.680939

Wattiaux, M. A. 2009. Signature pedagogy in agriculture. Exploring signature pedagogies: approaches to teaching disciplinary habits: approaches to teaching disciplinary habits of mind. 1st edition. Sterling, Virginia: Stylus Publishing, LLC; pp 207–223. Viewed 28 March 2021. https://books.google.com/books?id=0SWec-nwL4EC&printsec=copyright&source=gbs_pub_info_r#v=onepage&q=DOI&f=false.

Yuan, H. B., B. A. Williams, L. Yin, M. Liu, J. B. Fang, and D. Pang. 2011. Nursing students' views on the effectiveness of problem-based learning. Nurse Educ. Today. 31:577–581. doi:10.1016/j.nedt.2010.10.009