Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Control, Management, and Prevention of Bovine Respiratory Disease in Dairy Calves and Cows

Patrick J. Gorden, DVM[a,*], Paul Plummer, DVM, PhD[b]

KEYWORDS

• Bovine respiratory disease • Control • Management
• Dairy calves • Dairy cows

Despite advances in veterinary medicine, animal husbandry, and animal welfare, respiratory disease among dairy calves and cows continues to be a major problem for dairy producers. Although much of the effort is concentrated on controlling bovine respiratory disease (BRD) in young calves, also known as enzootic calf pneumonia (ECP), outbreaks of respiratory disease in adult animals can have negative effects on bovine welfare and production, resulting in devastating economic outcomes for dairy owners.

The United States Department of Agriculture National Animal Health Monitoring Service (NAHMS) has examined the incidence of respiratory disease in calves for more than 20 years (**Table 1**).[1] When evaluating respiratory disease statistics among dairy cattle, it becomes apparent that incidence of respiratory disease has not changed much since the early 1990s. Pre-weaned calf mortality has essentially been unchanged, ranging from a low of 7.8% in 2006 to 10.8% in 1996. The percentage of deaths attributed to respiratory disease in pre-weaned calves has also remained essentially unchanged during the same time period. A similar trend for mortality rate (range of 1.8%–2.2%) has been seen in weaned calves. There has been a substantial increase in the percentage of deaths credited to respiratory disease in weaned calves (34.8% to 46.5%).[1] In a separate study, Sivula and colleagues[2] reported a 7.6% morbidity rate and a 2.3% mortality rate from respiratory disease among calves between birth and 16 weeks of age. The attack rate of respiratory

[a] Food Supply Veterinary Medicine, Veterinary Diagnostic and Production Animal Medicine Department, Iowa State University College of Veterinary Medicine, 2432 Lloyd Veterinary Medical Center, 1600 South, 16th Street, Ames, IA 50011, USA
[b] Food Supply Veterinary Medicine, Veterinary Diagnostic and Production Animal Medicine Department, Iowa State University College of Veterinary Medicine, 2426 Lloyd Veterinary Medical Center, 1600 South, 16th Street, Ames, IA 50011, USA
* Corresponding author.
E-mail address: pgorden@iastate.edu

Vet Clin Food Anim 26 (2010) 243–259
doi:10.1016/j.cvfa.2010.03.004 **vetfood.theclinics.com**
0749-0720/10/$ – see front matter

Table 1
Changes in respiratory disease incidence 1991 to 2007

	1991	1996	2002	2007
Pre-weaned calf mortality	8.4	10.8	10.5	7.8
Percentage of deaths caused by respiratory disease pre-weaned calves	21.3	24.5	21.3	22.5
Weaned calf mortality	2.2	2.4	2.8	1.8
Percentage of deaths caused by respiratory disease–weaned calves	34.8	44.8	50%	46.5

Data from USDA. Dairy 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.

disease development in Minnesota dairy calves was 0.1 cases per 100 calf days during the same age range.

The costs associated with respiratory disease include prevention, treatment, and lost productivity. Several researchers have attempted to use available NAHMS data from their state to calculate a local cost of respiratory disease and respiratory disease prevention for specific management groups. For unweaned calves, estimates range from $9.84 to $16.35 per calf whereas weaned calf estimates range from $2.05 to $2.22 per calf.[3,4] Respiratory disease in the early stages of the calf's life can have significant effects on subsequent productivity and survivability, thus adding to these costs. A diagnosis of pneumonia during the first 6 months of life resulted in slower growth rates later in life[5] and decreased productivity.[2,6] Heifers followed through first calving that were diagnosed with respiratory disease as young calves were 2 or more times more likely to die before calving[7,8] and calve at an older age when compared with heifers that did not develop respiratory disease before 90 days of age.[8]

Diagnosis of pneumonia in adult dairy cattle is not as common as diseases such as mastitis, lameness, metabolic disease, and reproductive disorders. Annually, 3.3% of dairy cows develop owner-reported pneumonia and those pneumonia cases account for 11.3% of cow deaths.[9] Losses and prevention costs were estimated at $4.31 per cow in Michigan herds to $9.08 per cow in Ohio herds.[3,10] The Ohio study reported an estimated annual prevalence per 100 cow-years for pneumonia of 19% among adult dairy cattle.[10]

The lack of progress in controlling respiratory disease demonstrates that there continues to be significant room for improvement in controlling this multifactorial syndrome, and that dairy producers need assistance in applying evolving husbandry practices to improve dairy cattle health.

This article focuses on biosecurity programs to prevent respiratory disease in dairy calves and cows. Effective disease identification and treatment strategies are addressed.

PREVENTION OF RESPIRATORY DISEASE IN DAIRY CALVES

Prevention practices associated with respiratory disease control in calves include the development and maintenance of a robust immune system through delivery of adequate good-quality colostrum, sound nutrition, proper vaccination, biosecurity, and provision of adequate ventilation.

Minimizing Failure of Passive Transfer

The newborn calf is born with a naïve but functional immune system. Immune protection is dependent on consumption of preformed antibody. Failure of passive transfer (FPT) is a major factor in the development and severity of respiratory disease in calves.[5,11–17] Despite the significant effort placed on colostrum delivery to newborn calves, NAHMS Dairy 2007 determined that nearly 1 in 5 (19.2%) newborn heifer calves had FPT.[18] As part of complete program for respiratory disease control, practitioners must continually focus on colostrum management and monitor the incidence of FPT.

Associated with FPT are the environments that the calves are placed into, as these can have significant impacts on pneumonia as well. Assuring maternity pens are kept clean and dry and that calves are moved from maternity pens immediately after birth are important aspects of newborn care. Delivery of calves into a heavily contaminated maternity pen and leaving newborn calves in the maternity pen increases the risk that calves are orally exposed to bacterial pathogens.[19] Incidental consumption of environmental bacteria by the newborn calf is a risk factor for the development of enteric disease, and limits colostrum immunoglobulin absorption across the gut wall.[20,21]

Colostrum Collection and Storage

Colostrum must be collected, processed, and stored in a manner that limits bacterial contamination and minimizes bacterial incubation. Bacteria counts in colostrum can be assessed by performing a total plate count (TPC) and coliform counts. The goal is to have the TPC less than 1 million colony-forming units (CFU)/mL and the coliform count less than 10,000 CFU/mL.[22] Several methods have been used to reduce bacteria counts in colostrum while still maintaining adequate passive transfer, including pasteurization and acidification of colostrum using formic acid.[23–25] It should be noted that use of pasteurization and formic acid to control *Mycobacterium avium* subsp *paratuberculosis* (MAP) remains controversial and may not be appropriate for herds attempting to control Johnes disease.[23–28] Until further research is completed to more thoroughly characterize the importance of low numbers of MAP in treated colostrum samples, producers who are actively attempting to control or eradicate Johnes disease may wish to consider the use a colostrum replacement. For a more thorough discussion of colostrum replacers, readers are referred to an earlier issue of *Veterinary Clinics of North America*.[23]

Colostrum Delivery

An adequate volume of high-quality colostrum must be fed in a timely manner. Colostrum should contain at least 50 g IgG/L.[21] For typical Holstein calves (~85–90 lbs [38.5–40 kg]), 4 quarts (3.78 L) of colostrum should be fed as soon as possible after birth, preferably within 1 to 2 hours of birth.[29] Smaller calves such as Jerseys should be limited to 3 quarts (2.83 L) delivered in the same time frame. Colostrum delivered by a nurse bottle or esophageal feeder will result in adequate passive transfer[30–32] and provides assurance that the calf has consumed an adequate volume.

Navel Dipping

Navel dipping can play an important role in controlling diseases in newborn calves. Proper disinfection of navels has been shown to reduce calf mortality by half and reduce the percentage of calves treated for respiratory disease from nearly 19% in the nondisinfected group to 5% in the disinfected group (Donald Sockett, DVM, presentation notes, Land O Lakes, Webster City, IA, January 2010). To properly

perform naval disinfection, spraying of navels should be avoided, as this procedure does not provide adequate disinfection of the interior portion of the umbilical cord (Donald Sockett, DVM, presentation notes, Land O Lakes, Webster City, IA, January 2010). Dipping of the navel into a clean vessel containing fresh disinfectant provides better coverage of both the internal and external surface of the umbilicus.

Nutrition and Immune System Function

Adequate nutrition is essential for rapid growth and development of the young calf. Unfortunately, the definition of adequate has been somewhat blurred in the past in order to minimize the cost of milk-feeding programs. The immune system's nutrient consumption increases dramatically when responding to microbial challenges. Rates of gluconeogenesis increase 150% to 200% during moderate infections, and the basal metabolic rate has been shown to increase 25% to 55% during periods of sepsis in the human. Sepsis in laboratory rodents has resulted in a loss of approximately 40% of total body protein and reduction in rates of protein synthesis.[33] If nutrient intake is not optimal, calf growth and immune system functionality will be negatively affected.

Recent research has shown the potential growth ability of young calves and has demonstrated the importance of adequate nutrient intake on the function of the immune system. Godden and colleagues[34] compared the feeding of waste milk and milk replacer (MR), and demonstrated a reduction in respiratory disease mortality by feeding an equal volume of pasteurized waste milk compared with 0.45 kg of a 20% protein, 20% fat (20:20) MR per day. This finding should not be taken as endorsement of whole milk or pasteurized waste milk as the only liquid sources of increased energy and protein. There are several MR formulations on the market that will provide increased energy and protein compared with a 20:20 MR.

The effect of cold stress (4.7°C and 68.2% humidity) during the milk-feeding period has also been shown to increase respiratory disease scores and antibiotic treatments compared with calves not experiencing cold stress (15.5°C and 59% humidity).[35] Although further research is needed to fully understand the relationship between nutrient consumption and immune function, nutrition programs should be designed to maximize lean muscle gain and skeletal growth in order to fully support immune function and minimize respiratory disease.

Feeding Waste Milk

Feeding of waste milk increases growth rates of calves compared with the same volume of 20:20 MR.[34] However, feeding raw waste milk is a risk factor for *Mycobacterium bovis* colonization of the pharynx.[36] Pasteurization of waste milk has been shown to effectively reduce pathogenic bacteria associated with respiratory disease[37,38] but like colostrum, pasteurization remains controversial for the control of MAP.[27,34] Producers who are trying to control Johnes disease should avoid feeding waste milk until research is available that more completely characterizes the importance of low numbers of MAP in heat-treated milk.

Farms that use pasteurization of waste milk should monitor the effectiveness of the pasteurization process by using time- and temperature-monitoring equipment to assure a thorough process. In addition, TPC and coliform counts can be performed on pre- and post-pasteurization samples to assure adequate reduction in bacterial numbers. If pasteurized waste milk is not going to be fed immediately, particular attention needs to be paid to rapid and complete cooling followed by proper storage, because bacterial numbers can rapidly increase in warm milk.

Housing and Ventilation

Risk factors associated with housing calves and an increased incidence of respiratory disease include contact with or shared air space with older animals, relative humidity levels greater than 75%, poor air quality, increased stocking density, bedding type, bedding density, and power washing of calf facilities while calves are still present in the immediate area.[39,40] Housing management should be designed or modified to minimize risk factors associated with respiratory disease development.

The individual calf hutch placed in an outdoor environment often provides the best environment for the prevention of respiratory and other diseases of calves.[36,39,41] Calf hutches should be situated to minimize weather effects and should not be placed in proximity to other objects that can contaminate the calf's environment, such as building exhaust fan vents or runoff from neighboring animal lots. Hutches should be placed at least 4 feet (1.22 m) apart and thoroughly sanitized between uses. Ideally, hutches should be moved between groups to minimize bacterial contamination of the surface beneath the hutch.[36] Feeding and management practices should be organized to assure that animal contact moves sequentially from younger to older calves. Personnel who have been working with older animals should thoroughly disinfect clothing and hands before proceeding back into areas that house younger animals.

Ventilation of Unweaned Calf Barns

In an effort to improve worker comfort and reduce cold stress on animals, there has been an increase in the use of barns to house calves, especially on operations in the northern United States. Unfortunately, many of these barns have been designed to maximize calf numbers, resulting in space available per calf well below current recommendations of 2.2 to 3 m^2.[42] Ventilation systems are often designed with minimal regard for or understanding of the microenvironments created by individual housing of calves.[40] Investigations of risk factors for development of respiratory disease have demonstrated that there is often an association between increased bacteria counts in the air in the calf's microenvironment and increased incidence of respiratory disease.[40,43–46] Traditional tools used for evaluation of air quality, such as air meters to sense ammonia levels or manometers, have been found to be of little value in assessing risk for the development of respiratory disease.[40] Association between high bacteria counts in the air and the development of respiratory disease do not prove a causal relationship. In studies that have identified bacteria found in air it was determined that the majority of airborne bacteria are nonpathogenic, but even dead airborne bacteria can provide a burden on respiratory tract defenses that would make lung tissues more susceptible to infections.[47] Human work environments with high levels of nonpathogenic bacteria have been associated with a higher risk of the development of respiratory disease.[48]

Risk factors for increased bacteria counts in the air include high ambient temperatures, the use of solid-pen dividers and solid ends on calf pens, the use of bedding materials that provide a higher nesting score allowing calves to nest down into the bedding material to conserve heat (ie, straw), and smaller pen sizes per calf (<3 m^2). Humidity and ammonia levels were not found to have an effect on bacteria concentration in the air. Factors that were shown to decrease the prevalence of respiratory disease in calves include:

- Decreasing age of the individual calf
- Lower airborne bacteria counts
- Presence of solid dividers between calves
- Increased nesting score.[40]

The previous sentence is contradictory to an earlier sentence concerning risk factors of increased bacteria counts. Despite the fact that solid dividers and increased nesting score increased airborne bacteria counts, these factors are still protective as they reduce nose-to-nose contact and help the calf conserve energy.

Barns that are designed to house unweaned calves in individual hutches should be planned to provide the calf with at least 2.2 to 3 m^2 of total area per calf,[36,40,42] have solid dividers between calves, but maintain an open front and rear of the area where possible. Hutches should be bedded with material that allows the calf to adequately nest during periods of cold stress.[40,49] Addition of a positive pressure ventilation system that provides approximately 15 cubic feet per minute (CFM; 1 CFM = 0.028 m^3/min) of additional air per calf may help improve air quality enough to provide disease control similar to calf hutches and provide a comfortable work environment for workers.[49]

Ventilation of Group-Housed Calves

Although not commonplace in the United States, group housing of unweaned calves is becoming more prevalent, especially with the increased awareness of animal welfare and with computer milk-feeding stations being more readily available. Previous work has associated the use of computer milk feeders with an increased incidence of respiratory disease, although the role of stocking density was not evaluated in those trials.[50] More recent work has suggested that housing computer-fed calves in groups of 10 or less results in improved growth and less morbidity associated with respiratory disease.[51] These findings agree with others that have suggested limiting group size in both unweaned and weaned calves to groups of less than 7 results in the best overall welfare for the calves.[52] Further research is needed to determine whether this apparent group size effect is related to better social welfare of the calves in smaller groups or an effect of stocking density as a factor of barn volume. Stocking rate in a given volume of area is an important variable in total airborne pathogen load,[53,54] with a lower stocking rate reducing respiratory morbidity[6] (Thomas Earlywine, PhD, presentation notes, Land O Lakes, Webster City, IA, January 2010). Ventilation requirements do not have a linear relationship with stocking density. A twofold increase in stocking density requires nearly a tenfold increase in ventilation capacity to maintain pathogenic bacteria levels at similar concentrations.[54] This layout proves to be especially problematic in calf barns that are designed to be naturally ventilated or ventilated by negative pressure. These types of barns may not provide adequate ventilation at the level of the calf's environment. Positive pressure ventilation systems similar to those described in the previous section may be necessary to adequately ventilate buildings housing groups of unweaned and weaned calves.[49] Calves housed in buildings should have 2.3 to 2.8 m^2 or more of space available per calf.[42]

As calves age, positive pressure ventilation systems may become unnecessary as long as the ventilation system can provide even airflow throughout the building, and provide 4 air turns per hour in the winter and a minimum of 30 air turns per hour in the summer.[36,55]

Minimizing Weaning Stress

The process of weaning calves from milk and moving them into group housing is a very stressful period and often results in outbreaks of respiratory disease.[36,52,56,57] Weaning age is variable between calf raisers. Average weaning age in the United States is 8.2 weeks, with the majority of calves being weaned between 6 and 8 weeks of age.[18] There are various recommendations for determining when a calf is ready to be weaned, with most sources suggesting the calf is ready when consuming 1.5 to 2.5

lbs (680–1134 g) of calf starter per day for at least 2 to 3 consecutive days.[18,56] Using this benchmark will require that feed intake is monitored in calves approaching the intended weaning age.

There has been little work published on the best method to wean calves to minimize stress and associated respiratory disease. Some sources recommended not to move calves into group pens at the same time they are weaned but to give them 1 to 2 weeks in the individual pen after weaning to adjust fully to starter consumption.[57] A Minnesota trial saw no difference in growth rate between grouping calves immediately versus leaving calves in individual pens.[58] In contrast, an Italian trial reported that weaning calves at 49 days and immediately moving the calves to group housing resulted in higher growth rates and reduced respiratory treatments by one-half compared with weaning the calves and leaving them in individual hutches for 1 week.[56] In a separate trial, calves that were grouped at 49 days and fed MR 1 time per day for 1 week had a reduced incidence of respiratory disease compared with calves that were weaned at 49 days and then left in individual housing for 1 week (respective respiratory incidence = 20% vs 34%).[56] When calves are moved into group pens, it is important to allow them adequate space per calf, plenty of fresh air, and ready access to feed and water.[57]

An additional consideration when weaning calves should be to screen calves for signs of sickness. Calves that are clinically sick will be shedding large numbers of pathogenic organisms into the environment and are likely an important reservoir for introduction of disease to other calves.[36] Application of a screening method to consistently evaluate calves for sickness prior to weaning will reduce the number of calves that are inadvertently weaned with active respiratory disease.[59]

Metaphylaxis at Weaning

In beef feedlot production, the use of metaphylaxis at the time of movement to the feedlot has been successfully used to reduce the incidence of BRD.[11] Little work has been done regarding metaphylaxis in dairy calves until recently. Calves treated at weaning with a full dose of tulathromycin (Draxxin) were 50% less likely to develop BRD than calves administered approximately two-thirds the label dose of sustained-release oxytetracycline (Biomycin 200).[60] Veterinarians and producers should carefully evaluate the effectiveness of this practice, as it may lead to increased antimicrobial resistance. There were no negative controls in the study. For more information about metaphylaxis in cattle, see the article by Nickell and White elsewhere in this issue for further exploration of this topic.

Vaccine Programs in Young Calves

Effective vaccine programs for young dairy calves are difficult to develop because of the complex nature of the immature immune system of calves and the complexities of management systems in which the calves live. When developing vaccine programs, a risk assessment should be completed to determine the need for certain vaccines based on pathogen risks and breaks in immunity, such as FPT. The newborn calf has a functional immune system that is able to respond to antigens, provided maternal antibody is not present. Many of the native defense mechanisms have decreased activity in the first weeks to months of life.[61] If calves are at high risk for the development of disease due to high incidence of FPT in the herd, vaccination in the first month of life to develop antibody protection may be warranted.

One method for overcoming maternal antibody is to use vaccines administered at the mucosal surface, that is, intranasal (IN) vaccines. IN vaccines will result in the development of immune proteins (primarily IgA) on the mucosal surface where potential pathogens will be invading. This antibody will neutralize infectious agents at the

mucosal surface; thus preventing infection rather than just reducing severity of disease as is expected with parenteral vaccine administration. IN vaccine will also induce interferon release at the mucosal surface, which will provide a nonspecific antiviral environment and may stimulate maturation of the immune system.[61]

There is some consensus amongst calf consultants that the use of modified live vaccines in the first months of life will benefit the calf through the development of cell-mediated immunity; however, there is very little evidence to support this practice.[61] In these programs, calves are vaccinated several times during the first months of life, sometimes at intervals as close as 1 week. Extrapolating from research from other species, overvaccinating calves may lead to negative outcomes such as immunologic tolerance or autoimmunity.[61] A small body of evidence exists to support this immunologic response, but much more research is needed in this area to explore this practice.[62]

Vaccination programs should be designed to address the continuous-flow nature of most dairy operations as compared with seasonal vaccination patterns used in beef operations. It may be important to incorporate vaccines into breeding-age heifers prior to pregnancy if vaccines are not approved for pregnant animals. In addition, modified live infectious bovine rhinotracheitis (IBR) vaccines can cause necrosis of the corpus luteum, so IBR vaccines should not be administered close to breeding season in IBR-naïve animals.[63]

Immunology and vaccinology are rapidly developing fields of veterinary medicine, which should help answer some of the essential questions veterinarians have regarding development of effective vaccination programs for dairy calves. Readers are referred to the article by Ackermann and colleagues elsewhere in this issue for further exploration of this topic.

Quarantine Procedures for New Arrivals and Sick Animals

Off-site heifer raising and purchasing herd replacements represents a significant risk for the introduction of disease to the resident herd. At present, 9.3% of all dairy herds, representing 11.5% of heifers raised in the United States, are raised off-site. When heifers are raised off-site, approximately 63% of those heifers are comingled with cattle from other farms.[9] Approximately 39% of dairy operations brought some outside animals onto their farm during the previous year, including heifers raised off-site. On those operations, just over 20% of the farms quarantined animals from the resident population on arrival.[9] Incorporating quarantine facilities into dairy farm design plans is often overlooked even though it could provide insurance against disease proliferation. A written quarantine plan should be established that addresses caretaker and animal movement plans; and protocols for feeding, vaccination, disease testing, and facility disinfection to minimize the spread of disease between newly-arriving groups and the resident herd. If the dairy is purchasing lactating dairy cows, plans for milking cows in an isolated facility will also need to be made. Ideally, animals should be quarantined for a minimum of 14 to 21 days.[36]

Introduction of bovine viral diarrhea (BVD) into a dairy herd is often through a new heifer entering the herd, either home-raised or purchased.[41] Control of BVD outbreaks has been fairly well achieved through vaccination and other control programs. Persistently infected (PI) animals are an important reservoir of disease transmission.[36,64,65] As part of a complete biosecurity program for the prevention of respiratory disease, all new and returning herd arrivals should be tested by an appropriate screening test for the presence of virus in the submitted tissue as part of the quarantine process. In addition, in herds purchasing pregnant animals and herds trying to achieve BVD-negative status, calves should be tested at birth. For more information about BVD

control programs, readers should consult the article by Julia Ridpath elsewhere in this issue for further exploration of this topic.[66]

Housing of sick animals in a location away from healthy animals is an essential method for the control of disease spread on dairy farms. Animals that are clinically sick will be shedding large numbers of pathogenic organisms into the environment and are likely an important reservoir for introduction of disease to other animals,[36] especially immunocompromised animals such as young calves and peri-parturient cows. When selecting a site for the hospital facility, care must be taken to minimize contact with healthy animals and assure that the predominant airflow does not move toward clinically normal animals.

CONTROL AND MANAGEMENT OF RESPIRATORY DISEASE OUTBREAKS IN DAIRY CALVES

Veterinarians are not usually asked to evaluate individual sick calves unless there has been a history of respiratory disease in the past or there currently is an outbreak in which several calves are affected. To completely evaluate the disease process, a complete examination including collection of a thorough history should be completed, even if examining only one calf. Collection of history should facilitate the development of a list of all calf-rearing practices that could potentially have a negative impact on calf health. All responses should be validated with physical examinations, record analysis, and facilities evaluation, if possible. Record analysis can be used to determine previous morbidity and mortality rates and to assess whether there are patterns associated with certain seasons of the year or stocking rates. To complete the workup, the nutritional program, vaccination schedules, and treatment protocols should be examined. The calf caretakers' abilities to detect cases of respiratory disease should also be assessed.

Physical examinations should be performed on as many clinically-affected animals as are available to determine the range of clinical signs and to validate the true presence of respiratory disease. Many dairy producers do not recognize early signs of respiratory disease. Dairymens' diagnoses of pneumonia have been reported to have a sensitivity of 56% and a specificity of 100%.[2] Use of a screening system, such as the Calf Respiratory Scoring Chart, developed by veterinarians at the University of Wisconsin (UW) School of Veterinary Medicine (http://www.vetmed.wisc.edu/dms/fapm/fapmtools/calves.htm), can provide a more objective evaluation of clinical signs and provide a guideline for disease treatment. This screening system evaluates rectal temperature, nasal discharge, cough and ocular discharge, and ear position to assign an individual respiratory severity score for each calf. Validation of the screening system has been completed based on bronchoalveolar lavage (BAL) fluid cytology and culture. Calves that have a composite score of more than 4 are considered to have respiratory disease and should be treated accordingly.[59] Application of the UW screening system across all ages of available animals allows for the determination of age of onset of the respiratory problems, encouraging the calf caretaker to initiate therapy earlier in the course of the disease. The screening system can also be used to determine which calves need therapy, monitor treatment efficacy, and evaluate calf caretakers' ability to diagnose and treat calves. If used correctly, greater than 85% of calves that need to be treated should be correctly identified by calf caretakers.[59]

Selection of Therapeutic Agents

Selection of a therapeutic agent should be based on isolated or suspected etiologic agents based on previous experience with the herd. The most common bacterial

agents associated with ECP include *Pasteurella multocida, Mannheimia haemolytica, Histophilus somni,* and various *Mycoplasma* species.[2,17,36,39,65,67] Bovine respiratory syncytial virus (BRSV) and bovine coronavirus have been incriminated as primary agents in outbreaks of ECP.[17,39,65,67] Respiratory viruses (IBR, BVD, PI3, and BRSV) invade the upper respiratory tract tissues, resulting in the development of rhinitis, tracheitis, and/or bronchitis; this sometimes leads to the development of secondary bacterial invasion of the lower respiratory tract and the subsequent development of pneumonia.[41] However, there are many cases of ECP in which no virus pathogens are isolated from affected animals,[2,65] suggesting that viruses are not always involved in the development of ECP or that sampling occurs after optimal ability to detect virus.[2]

Diagnostic Methods to Assist Treatment Decisions

Necropsy can be an important diagnostic tool, but too often the wrong calves are selected to provide accurate diagnostic and therapeutic information. Performing necropsies on animals that are chronic poor doers or animals that would be classified as treatment failures should be avoided. Necropsies on such animals may result in the isolation of resistant strains of bacteria that may not truly represent the bacterial ecology of the initial pathogens. A more appropriate approach to using necropsy examinations would be to sacrifice acutely-affected animals. However, this should not be construed as a suggestion that necropsy examinations should not be completed if acutely-affected animals are not available for necropsy. Results of these examinations can provide critical information to determine deficiencies in management, such as nutritional insufficiency, and can be an important tool in client education. Necropsy examinations are essential for the diagnosis of aspiration pneumonia, which may be common in herds that are incorrectly using esophageal feeders to deliver colostrum, milk, or oral electrolytes.

Alternative methods to isolate the agents responsible for acute cases of ECP would be to use deep pharyngeal swabs, transtracheal wash (TTW), or BAL. Six acutely-affected animals should be selected for sampling based on physical examinations or the use of another screening method, such as the UW Calf Respiratory Scoring Chart.

Deep pharyngeal swabs can be done rapidly and are less invasive than TTW or BAL. Two or three individual swabs should be collected from each calf as described by McGuirk.[59] The number of swabs that should be collected per calf depends on type of diagnostic tests that will be performed; bacterial culture and sensitivity, mycoplasma culture, or viral detection. Presence of bacterial pathogens in high numbers, significant viral agents, or 2 or more swabs from the group of 6 testing positive for *Mycoplasma* spp is considered significant and can be used to direct treatment and management decisions. Comparative analysis between nasopharyngeal swabs and postmortem lung lavage has been used to validate the use of nasopharyngeal swabs in this manner. Positive predictive value for *M haemolytica* and *M bovis* was determined to be 100%. The negative predictive values were determined to be 67% and 33% for *M hemolytica* and *M bovis*, respectively. Genotypic analysis of matched isolates from nasopharyngeal swabs and lung lavage shows high degrees of similarity, demonstrating that the presence of bacteria on nasopharyngeal swabs is highly representative of lung etiology.[68] These results were obtained on clinical animals selected as described, and similar results would likely not be seen without appropriate case selection.

BAL or TTW can also be used to collect samples for culture, sensitivity, and viral detection, and can provide samples for cytologic evaluation of respiratory secretions.

Bacterial isolation of a homogeneous bacterial growth in excess of 10^6 CFU/mL or a positive *M bovis* culture is considered significant. Determination of leukocyte population by cytologic evaluation showing a decreased proportion of macrophages (<61%) or increased proportion of neutrophils (>39%) is considered indicative of an inflammatory response in the lung, even with a negative culture result.[59]

RESPIRATORY DISEASE IN ADULT DAIRY CATTLE

Despite the vast amount of literature concerning BRD in the dairy calf, there is nearly a complete paucity of information concerning adult dairy cattle. Incidence of pneumonia in the adult dairy animal is relatively low (3.3%)[9] but the proportional contribution to overall mortality on the dairy farm is 11.3%, indicating that response to therapy is relatively low. This lack of response may be caused by failure to recognize clinical disease early, or that these cases represent recrudescence of latent cases of ECP.

The concepts of control and prevention are very similar to the calf, but there are notable aspects that differ. Similarities include the maintenance of a functional immune system through delivery of sound nutrition, proper vaccination and minimal stress; biosecurity; and provision of adequate ventilation. The most notable difference between the 2 groups is the increased metabolic demand placed on the dairy cow through lactation.

Immune stress associated with parturition and lactation plays an important role in disease development.[69] Lymphocyte and neutrophil function decrease around the time of parturition[70,71] even though neutrophil numbers in the systemic circulation are increased.[69] The proportion of T lymphocytes is also altered, resulting in higher expression of T-suppressor cells around the time of calving and slower clearance of altered cells.[72,73] Stress introduced by negative energy balance and diseases such as ketosis[74–77] and hypocalcemia[72,78] make cows more susceptible to new and more severe infections during early lactation, including respiratory disease. Conditions that negatively affect dry matter intake and nutrient absorption, such as heat stress, subacute respiratory acidosis (SARA), and the inadvertent inclusion of mycotoxins in the diet may result in altered immune function and increased susceptibility to respiratory disease.[79–82] SARA can also have a direct effect on respiratory disease via caudal vena caval syndrome.[81]

Etiologic Agents and Diagnostic Procedures

The etiologic agents in the adult animal are similar to those mentioned for calves except that *M haemolytica* plays a more significant role in adult animals.[36,39] Herd workup procedures and diagnostic testing methods are also similar to those for the calf. Clinicians should pay particular attention to attempting to collect samples from acutely-affected animals in order to return results that are clinically relevant.[39,83] Clinicians should also assess overall herd health by doing a complete farm assessment to assure that conditions such as excessive negative energy and protein balance, ketosis, hypocalcemia, or SARA are not contributing to an increased incidence of respiratory disease.

Preventative Practices for Adult Dairy Cattle

Prevention practices associated with respiratory disease control in adult dairy cattle include immune system maintenance through sound nutrition, proper vaccination, and minimizing stress; biosecurity; and provision of adequate ventilation. Biosecurity practices for adult animals are similar to those in dairy calves. Readers should refer to the section on biosecurity earlier in this article for more discussion on the topic.

Maintenance of the Immune System

As discussed earlier, immune suppression is a major complication for disease prevention in adult dairy cattle. In addition to nutrition and management practices to minimize the effects of negative energy and protein balance as well as mineral insufficiency, husbandry practices must be maintained to maximize cow comfort and minimize stress. Such practices include prevention of overcrowding, minimizing pen moves, and averting social stress by incorporating management practices such as housing first-lactation cows separately from older cows. Discussion of nutritional and management practices that support a strong immune system and reduce stress are beyond the scope of this article. Readers should consult the article by Ackermann and colleagues elsewhere in this issue for further exploartion of this topic.

When designing vaccine programs for adult animals, a risk assessment of each individual dairy operation should be completed to determine the need for certain vaccines. These decisions should be based on pathogen risks and potential breaks in immunity, such as immune suppression associated with the periparturient period. To avoid immune suppression in the post-parturient period, it would be prudent to avoid administration of vaccines for at least 3 to 4 weeks after calving.[63] Consideration must be given to the need for transfer of colostral antibodies against disease threats of importance for the dairy. Vaccines should be administered at least 2 to 4 weeks before the expected calving date to avoid immune suppression,[70,71,77] thus providing sufficient time for immunoglobulin transfer to the colostrum to provide for adequate passive transfer.[23]

Ventilation

Ventilation systems need to be designed to limit the buildup of microbial agents, dust particles, noxious gases, heat, and humidity. Adult dairy cattle are minimally affected by cold stress caused by typical winter temperatures seen in the northern United States.[36] Barns may be underventilated during winter months to prevent freezing of water and manure systems, resulting in an increased incidence of respiratory disease. Ventilation systems should provide 36 CFM per 1000 lbs (454 kg) of body weight in cold weather and 335 CFM per 1000 lbs of body weight during hot weather.[84] An alternative method to assess ventilation function would be to determine the number of air exchanges per hour. During cold weather, 4 air exchanges must occur per hour whereas a minimum of 30 air exchanges per hour are needed during summer months.[36,55] Supplemental cooling will be necessary to minimize the effects of heat stress when the temperature heat index exceeds 72.[80,85]

SUMMARY

Incidence rates for BRD in dairy cattle have remained essentially unchanged over the last 20 years. Dairy calves are more commonly affected than adult animals, with BRD being the principal cause of death in weaned dairy calves. The lack of progress in controlling respiratory disease demonstrates that there continues to be significant room for improvement in controlling this multifactorial syndrome, and that dairy producers need assistance in applying evolving husbandry practices to improve the health of dairy cattle. Calf management programs that focus on the development of a robust immune system through adequate passive transfer, adequate energy and protein supply, sound biosecurity practices, and vaccination programs have helped alleviate problems on some herds. There is minimal information regarding control of respiratory problems in adult dairy cattle. Therefore, it seems prudent to focus the

management strategies on preventing disease through sound management of the transition period, along with sound vaccination and biosecurity programs.

ACKNOWLEDGMENTS

The authors would like to thank Drs Reneé Dewell and Leo Timms for their technical assistance in preparing the manuscript.

REFERENCES

1. USDA. Dairy 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.
2. Sivula NJ, Ames TR, Marsh WE, et al. Descriptive epidemiology of morbidity and mortality in Minnesota dairy heifer calves. Prev Vet Med 1996;27:155–71.
3. Kaneene JB, Hurd S. The national animal health monitoring system in Michigan. III. Cost estimates of selected dairy cattle diseases. Prev Vet Med 1990;8:127–40.
4. Sischo WM, Hird DW, Gardner LA, et al. Economics of disease occurrence and prevention on California dairy farms: a report and evaluation of data collected for the National Animal Health Monitoring System, 1986–1987. Prev Vet Med 1990;8:141–56.
5. Donovan GA, Dohoo IR, Montgomery DM, et al. Calf and disease factors affecting growth in female Holstein calves in Florida, USA. Prev Vet Med 1998; 33:1–10.
6. Bach A, Ahedo J, Kertz A. Using growth monitoring in heifer management and research [abstract]. J Dairy Sci 2008;91(E-Suppl 1):602.
7. Waltner-Toews D, Martin SW, Meek AH. The effect to early calfhood disease on survivorship and age at first calving. Can J Vet Res 1986;50:314–7.
8. Correa MT, Curtis CR, Erb HN, et al. Effect of calfhood morbidity on age at first calving in New York Holstein herd. Prev Vet Med 1988;6:253–62.
9. USDA. Dairy 2007, Part I: reference of dairy cattle health and management practices in the United States, 2007 Fort Collins (CO): USDA-APHIS-VS, CEAH; 2007 #N480.1007.
10. Miller GY, Dorn CR. Costs of dairy cattle diseases to producers in Ohio. Prev Vet Med 1990;8:171–82.
11. Van Donkersgoed J, Ribble C, Boyer LG, et al. Epidemiological study of enzootic pneumonia in dairy calves in Saskatchewan. Can J Vet Res 1993;57:247–54.
12. Blom JY. The relationship between serum immunoglobulin values and incidence of respiratory disease and enteritis in calves. Nord Vet Med 1982;34:276–84.
13. Thomas LH, Swann RG. Influence of colostrum on the incidence of calf pneumonia. Vet Rec 1973;92:454–5.
14. Williams MR, Spooner RL, Thomas LH. Quantitative studies on bovine immunoglobulins. Vet Rec 1975;96:81–4.
15. Davidson JN, Yancey SP, Campbell SG, et al. Relationship between serum immunoglobulin values and incidence of respiratory disease in calves. J Am Vet Med Assoc 1981;179:708–10.
16. Corbeil LB, Watt B, Corbeil RR, et al. Immunoglobulin concentrations in serum and nasal secretions of calves at the onset of pneumonia. Am J Vet Res 1984; 45:773–8.
17. Virtala AM, Grohn YT, Mechor GD, et al. The effect of maternally derived immunoglobulin G on the risk of respiratory disease in heifers during the first 3 months of life. Prev Vet Med 1999;39:25–37.

18. USDA. Dairy 2007, Heifer calf health and management practices on U.S. dairy operations, 2007. Fort Collins (CO): USDA: APHIS:VS, CEAH; 2010 #550.0110.
19. Villarroel A, Dargatz DA, Lane VM, et al. Suggested outline of potential critical control points for biosecurity and biocontainment on large dairy farms. J Am Vet Med Assoc 2007;230:808–19.
20. Poulsen KP, Hartmann FA, McGuirk SM. Bacteria in colostrum: impact on calf health. In: Proceedings of the 2002 American College of Veterinary Internal Medicine Forum, Dallas (TX). Ontario (CA): Content Management Corp 2002. p. 773.
21. Stewart S, Godden S, Bey R, et al. Preventing bacterial contamination and proliferation during the harvest, storage, and feeding of fresh bovine colostrum. J Dairy Sci 2005;88:2571–8.
22. McGuirk SM, Collins M. Managing the production, storage, and delivery of colostrum. Vet Clin North Am Food Anim Pract 2004;20:593–603.
23. Godden S. Colostrum management for dairy calves. Vet Clin North Am Food Anim Pract 2008;24:19–39.
24. Quirk Z, West J, Gorden PJ. Efficacy of formic acid as a means of controlling *Mycoplasma bovis* and *Mycobacterium avium* subspecies paratuberculosis in dairy cattle. In: Proceedings of the 41st Annual Meeting of the American Association of Bovine Practitioners, Charlotte (NC). Stillwater (OK): Frontier Printers Inc 2008. p. 279.
25. Anderson N. Experiences with free-access acidified-milk feeding in Ontario. In: Proceedings of the 41st Annual Meeting of the American Association of Bovine Practitioners, Charlotte (NC). Stillwater (OK): Frontier Printers Inc, 2008. p. 12–24.
26. Godden S, McMartin S, Feirtag J, et al. Heat-treatment of bovine colostrum. II: effects of heating duration on pathogen viability and immunoglobulin G. J Dairy Sci 2006;89:3476–83.
27. Peterson J, Godden S, Bey R. Relationship between bacteria levels in colostrum and efficiency of absorption of immunoglobulin G in newborn dairy calves. In: Proceedings of the 41st Annual Meeting of the American Association of Bovine Practitioners, Charlotte (NC). Stillwater (OK): Frontier Printers Inc 2008. p. 248.
28. Donahue M, Godden S, Bey R, et al. Preliminary results on the effect of feeding heat-treated colostrum on health and growth in pre-weaned dairy calves. In: Proceedings of the 42nd Annual Meeting of the American Association of Bovine Practitioners, Omaha (NE). Stillwater (OK): VM Publishing Co 2009. p. 187.
29. Bovine Alliance on Management and Nutrition. A guide to colostrum and colostrum management for dairy calves. revision. Available at: http://www.aphis.usda.gov/vs/ceah/ncahs/nahms/dairy/bamn/BAMNColostrum.pdf. 2001. Accessed January, 2010.
30. Molla A. Immunoglobulin levels in calves fed colostrum by stomach tube. Vet Rec 1978;103:377–80.
31. Adams GD, Bush LJ, Horner JL, et al. Two methods for administering colostrum to newborn calves. J Dairy Sci 1985;68:773–5.
32. Besser TE, Gay CC, Pritchett L. Comparison of three methods of feeding colostrum to dairy calves. J Am Vet Med Assoc 1991;198:419–22.
33. Lochmiller RH, Deerenberg C. Trade-offs in evolutionary immunology: just what is the cost of immunity? Oikos 2000;88(1):87–98.
34. Godden SM, Fetrow JP, Feirtag JM, et al. Economic analysis of feeding pasteurized nonsaleable milk versus conventional milk replacer to dairy calves. J Am Vet Med Assoc 2005;226(9):1547–54.

35. Nonnencke BJ, Foote MR, Miller BL, et al. Effects of chronic environmental cold on growth, health, and select metabolic and immunologic responses of pre-ruminant calves. J Dairy Sci 2009;92:6134–43.
36. Callan RJ, Garry FB. Biosecurity and bovine respiratory disease. Vet Clin North Am Food Anim Pract 2002;18:57–77.
37. Butler JA, Sickles SA, Johanns CJ, et al. Pasteurization of discard Mycoplasma mastitic milk used to feed calves: thermal effects on various *Mycoplasma*. J Dairy Sci 2000;83:2285–8.
38. Stabel JR, Hurd S, Calvente L, et al. Destruction of *Mycobacterium paratuberculosis*, *Salmonella* spp and *Mycoplasma* spp in raw milk by a commercial on-farm high-temperature, short-time pasteurization. J Dairy Sci 2004;87(7): 2177–83.
39. Woolums AR, Ames TR, Baker JC. The bronchopneumonias (respiratory disease complex of cattle, sheep, and goats). In: Smith BP, editor. Large animal internal medicine. 4th edition. St. Louis (MO): Mosby Elsevier; 2007. p. 602–52.
40. Lago A, McGuirk SM, Bennett TB, et al. Calf respiratory disease and pen microenvironments in naturally ventilated calf barns in winter. J Dairy Sci 2006;89: 4014–25.
41. Maunsell F, Donovan GA. Biosecurity and risk management for dairy replacements. Vet Clin North Am Food Anim Pract 2008;24:155–90.
42. Federation of Animal Science Societies. Dairy cattle. In: Guide for the care and use of agricultural animals in teaching and research. 3rd edition. Champagne (IL): Federation of Animal Science Societies 2010. p. 74–88.
43. Webster J. Environmental needs. In: Calf husbandry, health and welfare. Boulder (CO): Westview; 1984. p. 71–97.
44. Pritchard DG, Carpenter GA, Morzaria SP, et al. Effect of air filtration on respiratory disease in intensively housed veal calves. Vet Rec 1981;109:5–9.
45. Hillman P, Gebremedhin K, Warner R. Ventilation system to minimize airborne bacteria, dust, humidity, and ammonia in calf nurseries. J Dairy Sci 1992;75: 1305–12.
46. Blom JY, Madsen EB, Krogh HV, et al. Numbers of airborne bacteria and fungi in calf houses. Nord Vet Med 1984;36:215–20.
47. Wathes CM, Howard K, Jones CDR, et al. The balance of airborne bacteria in calf houses. J Agric Eng Res 1984;30:81–90.
48. Eduard W, Heederik D. Methods for quantitative assessment of airborne levels of noninfectious microorganisms in highly contaminated work environments. Am Ind Hyg Assoc J 1998;59:113–27.
49. Nordlund K. Practical considerations for ventilating calf barns in winter. In: Proceedings of 40th Annual Meeting of the American Association of Bovine Practitioners—Preconference Seminar 7B, Vancouver. Stillwater (OK): Frontier Printers Inc, 2007. p. 85–93.
50. Maatje K, Verhoeff J, Kremer WDJ, et al. Automated feeding of milk replacer and health control of group-housed veal calves. Vet Rec 1993;133:266–70.
51. Svensson C, Liberg P. The effect of group size on health and growth rate of Swedish dairy calves housed in pens with automatic milk-feeders. Prev Vet Med 2006;73:43–53.
52. Willard C, Losinger MS, Heinrichs AJ. Management variables associated with high mortality rates attributable to respiratory-tract problems in female calves prior to weaning. J Am Vet Med Assoc 1996;209:1756–9.
53. Nardell EA, Keegan J, Cheney SA, et al. Airborne infection: Theoretical limits of protection achievable by building ventilation. Am Rev Respir Dis 1991;144:302–6.

54. Wathes CM, Jones CD, Webster AJ. Ventilation, air hygiene and animal health. Vet Rec 1983;113:554–9.
55. Bates DW, Anderson JF. Calculation of ventilation needs for confined cattle. J Am Vet Med Assoc 1979;174(6):581–9.
56. Bach A, Ahedo J, Ferrer A. Optimizing weaning strategies of dairy replacement calves. J Dairy Sci 2010;93(1):413–9.
57. Quigley J. Calf Note #16—Stress at weaning. Available at: http://www.calfnotes.com. 2001. Accessed February, 2010.
58. Ziegler D, Ziegler B, Raeth-Knight M, et al. Performance of post weaned Holstein heifer calves transitioned to group housing using different management strategies while fed a common diet [abstract TH191]. J Dairy Sci 2008; 91(E-Suppl 1). F.
59. McGuirk SM. Disease management of dairy calves and heifers. Vet Clin North Am Food Anim Pract 2008;24:139–53.
60. Stanton AL, Kelton DF, LeBlanc SJ, et al. The effect of treatment with long-acting antibiotic at postweaning movement on respiratory disease and on growth in commercial dairy calves. J Dairy Sci 2010;93(1):574–81.
61. Chase CL, Hurley DJ, Reber AJ. Neonatal immune development in the calf and its impact on vaccine response. Vet Clin North Am Food Anim Pract 2008;24: 87–104.
62. Platt R, Widel PW, Kesl LD, et al. Comparison of humoral and cellular immune responses to a pentavalent modified live virus vaccine in three age groups of calves with maternal antibodies, before and after BVDV type 2 challenge. Vaccine 2009;27:4508–19.
63. Cortese V. Bovine vaccines and herd vaccination programs. In: Smith BP, editor. Large animal internal medicine. 4th edition. St. Louis (MO): Mosby Elsevier; 2007. p. 1591–603.
64. Shelton T, Hoffman B. Determining the prevalence of bovine viral diarrhea virus persistently infected calves originating from a number of modern western well-vaccinated dairy herds In: Proceedings of the 42nd Annual Meeting of the American Association of Bovine Practitioners, Omaha (NE). Stillwater (OK): VM Publishing Co 2009. p. 182.
65. Angen O, Thomsen J, Larsen LE, et al. Respiratory disease in calves: microbiological investigations on trans-tracheally aspirated bronchoalveolar fluid and acute phase protein response. Vet Microbiol 2009;137:165–71.
66. Smith S. BVD control for the dairy practitioner: Strategies and implementation. In: Proceedings of the 42nd Annual Meeting of the American Association of Bovine Practitioners, Omaha (NE). Stillwater (OK): VM Publishing Co 2009. p. 98–102.
67. Baker JC, Werdin RE, Ames TR, et al. Study on the etiologic role of bovine respiratory syncytial virus in pneumonia of dairy calves. J Am Vet Med Assoc 1986; 189:66–70.
68. Godinho KS, Sarasola P, Renoult E, et al. Use of deep nasopharyngeal swabs as a predictive diagnostic method for natural respiratory infections in calves. Vet Rec 2007;160:22–5.
69. Kimura K, Goff JP, Kehrli ME Jr. Effects of the presence of the mammary gland on expression of neutrophil adhesion molecules and myeloperoxidase activity in periparturient dairy cows. J Dairy Sci 1999;82:2385–92.
70. Kehrli ME Jr, Nonnecke BJ, Roth JA. Alterations in bovine neutrophil function during the periparturient period. Am J Vet Res 1989;50(2):207–14.
71. Kehrli ME Jr, Nonnecke BJ, Roth JA. Alterations in bovine lymphocyte function during the periparturient period. Am J Vet Res 1989;50(2):215–20.

72. Kimura K, Goff JP, Kehrli ME Jr, et al. Effects of mastectomy on composition of peripheral blood mononuclear cell populations in periparturient dairy cows. J Dairy Sci 2002;85:1437–44.
73. Shafer-Weaver KA, Sordillo LM. Bovine $CD8^+$ suppressor lymphocytes alter immune responsiveness during the postpartum period. Vet Immunol Immunopathol 1997;56:53–64.
74. Goff JP, Horst RL. Physiological changes at parturition and their relationship to metabolic disorders. J Dairy Sci 1997;80(1):176–86.
75. Perkins KH, VandeHaar JM, Burton JL, et al. Clinical responses to intramammary endotoxin infusion in dairy cows subjected to feed restriction. J Dairy Sci 2002; 85:1724–31.
76. Moyes KM, Drackley JK, Salak-Johnson JL, et al. Dietary-induced negative energy balance has minimal effects on innate immunity during a *Streptococcus uberis* mastitis challenge in dairy cows during mid-lactation. J Dairy Sci 2009; 92:4301–16.
77. Kremer WD, Noordhuizen-Stassen EN, Grommers FJ, et al. Severity of experimental *Escherichia coli* mastitis in ketonemic and nonketonemic dairy cows. J Dairy Sci 1993;76:3428–36.
78. Kimura K, Reinhardt TA, Goff JP. Parturition and hypocalcemia blunts calcium signals in immune cells of dairy cattle. J Dairy Sci 2006;89:2588–95.
79. National Research Council. Dry matter intake. In: Nutrient requirements of dairy cattle. 7th edition. Washington, DC: National Academy Press 2001. p. 3–12.
80. Collier RJ, Dahl GE, VanBaale MJ. Major advances associated with environmental effects on dairy cattle. J Dairy Sci 2006;89:1244–53.
81. Kleen JL, Hooijer GA, Rehage J, et al. Subacute rumen acidosis (SARA): a review. J Vet Med A Physiol Pathol Clin Med 2003;50:406–14.
82. Whitlow L. Mold and mycotoxin issues in dairy cattle: effects, prevention, and treatment. Available at: http://www.extension.org/pages/Mold_and_Mycotoxin Issues_in Dairy_Cattle:_Effects,_Prevention_and_Treatment. 2009. Accessed January, 2010.
83. Divers TJ. Respiratory disease. In: Divers TJ, Peek SF, editors. Rebhun's diseases of dairy cattle. 2nd edition. St. Louis (MO): Saunders Elsevier; 2008. p. 78–129.
84. Midwest Plan Service. Mechanical ventilating systems for livestock housing. 1st edition. Ames (IA): Midwest Plan Services-32. Iowa State University; 1990. 50011.
85. Brouk MJ, Smith JF, Harner III JP. Managing the cow environment for improved animal health and milk quality. In: NMC 43rd Annual Meeting Proceedings, Charlotte (NC). Madison (WI): Omnipress 2004. p. 271–81.