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Biosecurity and bovine respiratory disease

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Respiratory disease problems represent a major area of concern for all phases of cattle production. All types and all ages of cattle are susceptible to respiratory problems, and in some production settings, respiratory disease is the single most important cause of livestock morbidity and mortality. In recent national surveys, respiratory disease is reported to account for 24.5% of preweaned dairy heifer calf deaths, and it is the leading cause of death in weaned heifer calves, accounting for 44.8% of calf death losses [54]. In adult dairy cows, respiratory disease is less important than mastitis, lameness, metabolic diseases, and reproductive disorders as a cause of morbidity, but it still affects 2.5% of adult dairy cattle on a yearly basis, and 9.6% of dairy cow deaths are attributed to respiratory disease [54]. In preweaned beef calves over 3 weeks of age, respiratory problems represent 21% of health problems, occurring in approximately 0.8% of all calves [52]. Respiratory disease accounts for 16.3% of total beef calf death loss and 6.0% of total breeding cattle death loss on cow–calf operations [52]. Shipping fever was recently reported to occur in 14.4% of feedlot cattle, and this respiratory problem was more than 4 times more prevalent than the next leading cause of morbidity, which was acute interstitial pneumonia [56]. Annual death loss estimates due to respiratory disease for all cattle and calves in the United States exceed 1.2 million animals, with an estimated total economic loss greater than $478 million [53].

These morbidity and mortality estimates underscore the tremendous importance of respiratory disease to cattle producers. Considerable effort over many years has been focused on improving our understanding of this problem. Despite improvements in our understanding of pathogenesis, characteristics of causative agents, vaccine technology, and means of prevention

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and treatment, it seems that respiratory disease remains one of the foremost cattle health concerns.

The challenge that the authors were presented with in writing this article was to consider the role that biosecurity could play in reducing the occurrence or effect of respiratory disease. It seems that little research has specifically evaluated the effects of biosecurity management practices on the occurrence of the problem in livestock operations. Indeed, recognizing the multifactorial etiology of infectious respiratory disease and the ubiquitous presence of the pathogens involved leads to the conclusion that attempts to decrease disease prevalence must incorporate multiple management steps, of which biosecurity practices are only a single component. Although biosecurity practices have equal potential to decrease respiratory disease losses in all food animal species, the authors focus this article primarily on bovine respiratory disease complex. This article addresses major areas of respiratory pathogen control and provides some suggestions for practical intervention.

Overview of bovine respiratory disease

Bovine respiratory disease is not a single entity, nor is it attributable to a single cause [2]. One useful scheme for characterizing respiratory tract diseases in a practical manner distinguishes three different categories of problems [40]. These include the bovine respiratory disease complex (BRDC), epitomized by shipping fever pneumonia and enzootic calf pneumonia; acute interstitial pneumonias; and metastatic pneumonia. This scheme excludes many problems that involve only the upper respiratory tract, although these problems may predispose to lower tract infections. The interstitial pneumonias are most commonly attributed to toxicoses, and metastatic pneumonias are secondary complications of disease in other organ systems that spread hematogenously to the lung. Although these disease problems are frequently fatal for affected cattle, they occur sporadically and are generally not considered to be contagious. The authors focus their attention for this discussion on BRDC. This problem has an infectious origin, and it is by far the most frequently occurring form of cattle respiratory disease. Cattle of all ages and in a variety of circumstances can be affected by BRDC, but the disease most commonly manifests in young dairy calves (enzootic calf pneumonia) and in beef calves recently arrived at feedlots (shipping fever pneumonia).

Research over the past several decades has provided an increasingly clear picture of how BRDC occurs and why it is so common. Unfortunately, this knowledge has not led to a commensurate decrease in the morbidity and mortality associated with this problem, primarily because animals are commonly managed in ways that predispose to disease development.

Bovine respiratory disease complex refers to bacterial bronchopneumonia that may or may not be complicated by previous or concurrent viral or

Mycoplasma infection [2]. Numerous bacterial species can be isolated from the lungs of affected animals. In feedlot cattle and adult cattle, *Mannheimia (Pasteurella) haemolytica* is considered the most important pathogen, with lesser roles attributed to *Pasteurella multocida* and *Hemophilus somnus*. In younger calves, these same pathogens play a role, but *Mycoplasma* spp. are also considered to be important. *Arcanobacterium pyogenes, Fusobacterium* spp., and *Bacteroides* spp. are frequently isolated from animals with chronic, abscessing lung lesions but do not play a major role in acute bronchopneumonia. Less common bacterial isolates, including *Streptococcus* spp., *Staphylococcus* spp., *Pseudomonas aeruginosa*, and *Chlamydia* spp., are also occasionally identified in young calves.

All of the bacterial pathogens considered important in BRDC can be isolated from the upper respiratory tract of healthy cattle and calves. These pathogens are considered ubiquitous in cattle populations, not because they can be found in each animal, but because they are readily identified in the nasopharynx of some animals in most populations. In the absence of other predisposing causes of disease, it seems that the simple presence of these bacterial agents is not of major significance. The disease complex is best characterized as being multifactorial, only occurring when a combination of factors involving the animal, environment, and infectious agents are present.

Viral pathogens are implicated in the development of BRDC, although the final pulmonary pathology is primarily caused by bacterial pathogens [2]. The principal viruses involved in BRDC include bovine herpesvirus 1 (infectious bovine rhinotracheitis), bovine parainfluenza virus type 3, bovine respiratory syncytial virus, and bovine viral diarrhea virus. Lesser roles are attributed to bovine coronavirus, adenovirus, rhinovirus, reovirus, and enterovirus. These viral pathogens primarily infect the upper respiratory tract, resulting in rhinitis, tracheitis, and bronchitis. Their ability to cause direct pulmonary disease is generally limited except for bovine respiratory syncytial virus, which can also cause severe lung damage as the primary agent. All of these viral pathogens predispose the lung to bacterial infection and bronchopneumonia. The primary role of these agents in BRDC is to promote bacterial challenge to the lungs by compromising respiratory tract defense mechanisms.

The predisposing causes of BRDC act synergistically and are most commonly identified in combination rather than as single causative problems. The list of predisposing animal factors is long and includes animal age, decreased immune responsiveness due to animal stress, lack of previous viral exposure or vaccination, inadequate passive immunoglobulin transfer in young calves, nutritional deficiencies, and dehydration. Environmental risk factors include high air humidity or dust content, rapidly changing environmental temperatures, extreme heat or cold, and high concentrations of noxious gases such as ammonia. Several risk factors may increase pathogen density or pathogen exposure, although these risk factors probably act by other means as well. For example, commingling cattle from multiple sources may increase exposure to antigenically heterogeneous viral pathogens, while also increasing animal stress. Poor ventilation and high humidity can increase pathogen density and survival time but also can increase noxious gas concentrations and adversely affect pulmonary function. Animal crowding increases airborne pathogen exposure but also induces animal stress and reduces immune responsiveness.

Prevention of bovine respiratory disease complex

When evaluating the rate of BRDC occurrence in cattle populations, it is clear that efforts to prevent this disease have not been effective on an industry-wide basis, although some individual producers have successfully used prevention strategies. The two biggest areas of BRDC effect are in the form of enzootic calf pneumonia of dairy calves and shipping fever pneumonia of feedlot cattle. Given our current understanding of this disease problem, it is clear that the animal management systems employed for these groups of animals (i.e., dairy calf–rearing systems and feedlot cattle–receiving systems) have failed to rigorously apply knowledge of disease pathogenesis and prevention into their processes. This situation may be changing currently, as the beef production industry increasingly uses quality-assurance principles in production systems and develops marketing procedures and animal-purchasing practices that reward improvements in animal health [12,35,46]. Similarly, the dairy industry has begun to recognize the economic benefit of improved calf health and increasingly uses specialized calf-rearing systems [1,44].

Because the purpose of this article is to examine the role of biosecurity management in respiratory disease prevention, the authors do not attempt to provide a complete review of BRDC preventive practices. Many of the important means of preventing BRDC do not employ biosecurity but are targeted toward enhancing animal immune preparedness and enhancing animal response to infectious challenge. Effective respiratory disease preventive practices are those targeted at reducing identified risk factors for disease development [1,2,35,46]. These practices include management to improve animal nutrition with special emphasis on micronutrient nutrition, practices that reduce animal stress, reduced commingling of animals, improved animal transportation and feedlot receiving practices, improved preconditioning and vaccination programs that emphasize vaccination before shipment and during times of low calf stress, and improved ventilation with reduced crowding.

It is important to consider the factors that drive the development and implementation of disease prevention and biosecurity programs. The most apparent of these factors is the effect on animal production and growth; however, all interventions have their cost, and these costs must always be considered relative to the potential economic returns. Unfortunately, information regarding the financial impact of herd biosecurity programs is limited, and estimates based on clinical experience must often be applied. Other issues, including herd pathogen status and its effect on livestock marketing, food product quality assurance, drug residues, injection site lesions, antimicrobial resistance, and animal welfare also contribute to the forces that drive the development of biosecurity programs. Ultimately, a biosecurity program must be integrated into the overall herd management. It must be developed using a team approach that addresses the concerns of the producer, the economic effect on the production unit, the influence on product quality, and public health concerns. The veterinarian is best suited to effectively develop and implement such programs.

The multifactorial nature of BRDC and the ubiquitous presence of respiratory pathogens are important concepts when considering the role that biosecurity can play in decreasing the prevalence of disease. For infectious diseases in which point source pathogen exposure, high susceptibility, and high virulence are prominent features of disease transmission (e.g., anthrax, foot-and-mouth disease, rabies, and so forth), limiting animal contact with the pathogen is a key feature of disease prevention and may even provide the means of disease eradication. Alternatively, when the causative pathogens are endemic in a population and individual susceptibility is dependent on numerous interrelated factors, the management of animal resistance and risk factors may be proportionally more important for disease prevention than biosecurity practices. It appears that BRDC prevention requires a combination of management to enhance animal resistance plus management to reduce exposure to the pathogens. The important point is not to de-emphasize the value of reducing pathogen introduction, exposure, and transmission (i.e., biosecurity) but to also stress the importance of other management features that promote animal resistance. It is particularly important that preventive management practices be coordinated and used in combination, because no single management procedure will be successful without the complement of other practices. It is likely that our inability to reduce the prevalence of respiratory disease in cattle is, in part, attributable to our failure to integrate multiple aspects of respiratory disease prevention practices, including biosecurity.

The fundamental concept of biosecurity is to decrease pathogen transmission between animals. Transmission of respiratory pathogens occurs by close nose-to-nose contact, environmental or fomite exposure, and airborne exposure. Increased contact between shedding and susceptible individuals increases pathogen spread. Environmental exposure through common areas and equipment that involve oral or nasal contact such as feed bunks, water troughs, and salt blocks may be an even greater risk, however.

Total environmental pathogen load is extremely important in considering respiratory pathogen transmission. Environmental contamination from animals in contact is the primary source of most respiratory pathogens. Individual animal shedding is quite variable and depends on the etiologic agent, the time course of the disease, the clinical severity, and the immune response of the host. In general, clinically ill animals shed greater numbers of pathogens than normal or asymptomatic animals; however, it must be recognized that individuals periodically shed both viral and bacterial respiratory pathogens without evidence of disease. Well-vaccinated animals may also periodically shed pathogens and should not necessarily be considered completely safe from disease transmission.

The persistence of the pathogen in the environment also contributes to pathogen exposure. Environmental pathogen survival times depend on many factors, including organic material, moisture, direct sunlight, and exposure to disinfectants. Environmental survival times for most viral respiratory pathogens are probably on the order of minutes to several hours [18,47]. Survival times for bacterial pathogens may be longer depending on the environmental conditions and the organism. Airborne transmission is dependent on numerous factors, including ambient temperature, relative humidity, airborne particle (dust) density, ventilation, prevailing wind, and structural or geographic obstructions [47]. Airborne transmission of typical viral respiratory pathogens can occur over distances as far as 4 meters and possibly further [29,30]. Airborne transmission of other viruses such as foot-and-mouth disease virus or pseudorabies virus has been shown to occur over many miles, however [10,11,15,45,47]. Adding to the complexity of pathogen transmission, it seems that the efficiency of transmission is different between different strains of a given pathogen [30]. Understanding how management practices can reduce either pathogen shedding or exposure is the key to creating effective biosecurity programs.

Biosecurity and bovine respiratory disease complex

The term *biosecurity* is used for those management and hygiene practices that reduce introduction, exposure, and transmission of infectious agents. Although biosecurity may not provide the single most important component of respiratory disease prevention, reducing pathogen exposure is a valuable part of any infectious disease management system. Little information is available to specifically evaluate the effect of individual biosecurity practices in prevention of BRDC, but there are some important respiratory disease prevention practices that limit pathogen exposure and good reason to more closely evaluate the role that biosecurity could play in the future. The authors emphasize five areas of biosecurity management that should be more rigorously applied for the reduction of respiratory disease prevalence in cattle, including (1) strategic vaccination, (2) calf biosecurity, (3) housing ventilation, (4) commingling and animal contact, and (5) bovine viral diarrhea virus control.

Strategic vaccination

Many improvements in vaccine technology have occurred over the past few decades, and practitioners have an array of improved bovine respiratory pathogen vaccines at their disposal [35]. Unfortunately, the current respiratory pathogen vaccines have not all been scrutinized for efficacy to the most desirable degree, and many do not protect against respiratory disease nearly as effectively as some veterinarians and producers would like to believe. Although vaccines directed at specific conserved proteins, such as toxoid vaccines, may completely prevent a particular disease, vaccines against complex disease agents that have multiple antigenic strains are unlikely to be capable of such levels of protection. Respiratory vaccines are better viewed as disease modifiers than absolute preventive agents.

Vaccines are usually used as a means to decrease the likelihood or severity of disease occurrence in the individual animal receiving the vaccination. Indeed, vaccine efficacy may be evaluated in many ways, but the more rigorous evaluations involve the ability of a vaccinated animal to withstand a challenge of disease or pathogen exposure [42]. Practitioners tend to view vaccination as one of the management factors that enhance animal resistance to infection and thus augment the value of biosecurity management by working to reduce susceptibility to infectious disease rather than decrease exposure and transmission. For respiratory disease prevention, however, effective vaccination can also serve as part of a biosecurity management system. In addition to preventing disease, a vaccine's efficacy might also be considered for its ability to limit pathogen shedding when infection does occur. Vaccine-induced immunity often results in decreased magnitude and duration of pathogen shedding [6,16,59]. Because exposure is directly related to pathogen concentration in the environment, it follows that vaccine-induced reductions in shedding should decrease transmission within a susceptible population.

Proper vaccine use and a well-managed vaccination program can be viewed as part of a complete biosecurity program. At a minimum, a good vaccination program should include the following:

- Proper storage and administration of the vaccine as indicated by the manufacturer's labeled recommendations.
- Vaccination of all susceptible animals, including both resident and incoming animals.
- Application of the vaccine to systemically healthy, well-nourished, minimally stressed, and immunocompetent cattle.
- Strategic timing of vaccination so that it precedes contact with new animals long enough to allow an appropriate immune response.
- Revaccination as recommended for the particular vaccine product.

Calf biosecurity

Biosecurity management of calves is extremely important for development of healthy animals. Many of the biosecurity recommendations for newborn calves focus on decreasing the transmission of enteric pathogens; however, these same principles can be important for minimizing respiratory disease problems. Several details of calf biosecurity management deserve emphasis.

Environmental and housing factors significantly affect calf health and viability. Differences in calf management for cow–calf herds versus dairies are related to the relative risk of respiratory disease between these two production groups. Beef calves are generally raised in open-range situations that effectively dilute the exposure to respiratory pathogens. Although beef calves are continually exposed to pathogens shed from adult cattle and other calves, the magnitude of pathogen exposure before weaning is generally low, resulting in relatively little respiratory disease. In contrast to many enteric pathogens, the environmental survival time of the respiratory pathogens is limited [18], and accumulation of pathogens in the environment is not considered a primary concern.

Dairy calf housing has a significant effect on the incidence of respiratory disease in neonatal calves. Although the common viral respiratory pathogens can be transmitted over distances up to 4 meters [29,30], properly spaced calf hutches seem to effectively limit aerosol transmission of respiratory pathogens. The short survival of these pathogens in the environment limits the transmission between successive occupants of an individual hutch. Disinfection procedures that are used for enteric diseases should be more than sufficient to decrease respiratory pathogen transmission (see article by Barrington et al. in this issue). In contrast, there is a high risk of respiratory disease transmission in group-raised neonatal calves. Factors including the number of animals, relative animal density, housing facilities, and ventilation conditions significantly contribute to transmission in grouped calves and are discussed in subsequent sections of this article.

Numerous management practices can decrease exposure and transmission of respiratory pathogens to calves in dairy operations. Feeding pasteurized milk or milk replacer is a useful biosecurity practice for minimizing the spread of enteric agents such as *Salmonella* spp. or *Mycobacterium avium* subsp. *paratuberculosis*. These practices are also effective at limiting ingestion of potential respiratory pathogens. *Mycoplasma* spp. bacteria are commonly implicated in newborn calf disease, including enzootic calf pneumonia [2,37,48,49]. Although *Mycoplasma* spp. may spread by the airborne route, it is also a common mastitis pathogen and can be shed from clinically or subclinically infected cows [24,37,49]. Nasopharyngeal colonization occurs after oral ingestion of contaminated milk, potentially resulting in clinical respiratory disease in calves [37]. *Mycoplasma* spp. and other pathogens can also spread hematogenously after ingestion by a susceptible calf [24,37]. Similarly, other potential respiratory pathogens such as *Streptococcus* spp., *Staphylococcus* spp., *Salmonella* spp., and *Escherichia coli* can be recovered from milk and spread hematogenously to the lungs after oral ingestion. Bovine viral diarrhea virus is shed in the milk of persistently infected cattle. Ingestion of bovine viral diarrhea virus–contaminated milk can result in respiratory and systemic infections, possible immune suppression, and respiratory disease.

Proper cleaning and disinfection of calf feeding equipment, including nursing bottles, buckets, and mixing utensils, should be performed. Equipment should be cleaned with a detergent and disinfected between uses. A common and economical disinfectant is standard household bleach used at a 1:10 dilution. Bottles and equipment that are potentially shared between multiple animals should be soaked for 15 to 20 minutes in this solution. Although bleach will not completely kill all potential pathogens, it is effective at significantly decreasing viable numbers and thus contributing to decreased exposure and transmission between feedings.

Prompt removal of dairy calves from the maternity pen environment, where they are exposed to numerous adult cow pathogens, can also decrease transmission of potential respiratory pathogens. Newborn calves should not have direct contact with older calves and adults. Calf hutch spacing should be evaluated, with a minimum of 4 feet of separation between calves. Worker hygiene can minimize contamination of calf feed and the calf environment. Appropriate vaccination of dams before colostral production can increase passive transfer of effective antibodies, reducing the risk of exposure and potential shedding after infection. It has been demonstrated that good colostral transfer to beef calves was associated with decreased occurrence of disease episodes and improved calf performance all the way through the growing and finishing period in feedlot animals [36]. It is unlikely that the passive transfer of immunoglobulins per se is specifically responsible for beneficial effects on the long-term health of animals, but profound effects may result from management that improves newborn health and disease resistance. This in turn provides for improved nutrition, growth, physiologic well-being, and decreased total pathogen load.

Numerous calfhood husbandry procedures should be considered as standard biosecurity protocols for all infectious diseases, including respiratory disease. Sick animals should be identified and separated from healthy animals. A specific calf-isolation area should be established, with consideration to animal comfort and ease of cleaning and disinfection. Where practical, individual equipment should be used for each separate calf. Specific care and treatment personnel should be identified, and animals with suspected infectious diseases should be treated after handling healthy animals. Additional personnel hygiene protocols include dedicated coveralls to be used in the sick pens, the use of rubber overboots, and disinfectant footbaths. Personnel should be encouraged to wash their hands before and after entering the sick pens and between caring for animals with dissimilar disease conditions. In many cases, equipment and facilities need to be made available to help establish such procedures.

Similar biosecurity management practices can be used in cow–calf herds. Although feeding pasteurized milk or milk replacer is obviously not a practical management practice, milk-borne exposure to pathogens can be minimized by proper attention to the adult cows. Adult cattle must be appropriately vaccinated to provide optimal colostral immunity to the calves and to decrease adult cow infections and shedding. Adult cow nutrition should be optimized to improve colostrum quality. Adult cow nutrition can also have a dramatic effect on calving ease and decrease the incidence of dystocia. Special attention should be placed on high-risk calves, including calves delivered with manual assistance, cesarean section, born in inclement weather, weak or premature calves, and multiple births. Such calves often do not nurse colostrum in a timely fashion or have impaired absorption of immunoglobulin. Cows should be evaluated for evidence of clinical mastitis and treated or culled as appropriate. Decreased morbidity can be observed by minimizing the time that beef cow–calf pairs spend in a designated calving area, where pathogen loads tend to increase throughout the calving season. Bovine viral diarrhea virus surveillance and eradication in cows and calves should also be used (see discussion in a following section).

As can be seen from the preceding discussion, many of the management practices that contribute to biosecurity of respiratory disease are standard quality-assurance practices that are recommended for basic calf health.

Ventilation

Good ventilation is a critical aspect of animal management and can profoundly affect respiratory health. Several discussions of ventilation and its effect on animal health are present in the literature [2–5,13,14,19,27,31, 34,38,39,43,51,58]. Proper ventilation serves eight primary functions:

1. It decreases the airborne pathogen concentration
2. It eliminates noxious gases (ammonia, hydrogen sulfide, carbon dioxide, carbon monoxide, and methane)
3. It decreases airborne dust contamination
4. It decreases airborne endotoxin levels
5. It maintains optimum ambient temperature
6. It maintains optimum environmental humidity levels
7. It eliminates drafts
8. It eliminates areas of stagnant air

With respect to biosecurity, one of the most important aspects of proper ventilation is the reduction in the concentration of airborne pathogens. All of the important viral and bacterial respiratory pathogens can spread aerogenously and can attain high concentrations in poorly ventilated housing areas. Airborne pathogen concentration is a function of many factors, including animal type, housing system, stocking rate, bedding, humidity, dust particle density and size, and finally, elimination through ventilation. Improved ventilation is one important means whereby airborne pathogen concentration can be readily decreased within the given constraints of an operation; however, pathogen removal is not a linear function, and practical and theoretical limits are often observed [33]. Studies of building ventilation for humans demonstrate potential reductions in airborne exposure of pathogens and disease incidence, although improved ventilation beyond that which provides comfort may not be practical or provide significant additional benefit [33]. As the airborne pathogen load rises, ventilation provides progressively less protection against respiratory infections. It is important to realize that stocking rate has a more dramatic effect on airborne pathogen density than ventilation [33,58]. For example, a two-fold increase in stocking rate requires nearly a 10-fold increase in ventilation to maintain the same airborne pathogen density [58]. Ventilation cannot overcome grossly inadequate housing, management, or hygiene within a production unit.

Along with stocking density, there are other practical concerns that contribute to airborne pathogen density and transmission. One of these is related to animal handling and excitement. It is extremely important to handle grouped animals in a calm environment with minimal animal activity and stress. Increased animal activity not only increases dust exposure (which contains airborne pathogens) but also increases ventilatory rate, ventilatory effort, and tidal volume, which in turn increases the amount of aerosolized pathogen shed by infected animals and the amount of pathogen inhaled by susceptible animals. The increased dust exposure will also adversely affect mucociliary clearance and respiratory defense mechanisms.

Part of the effect of ventilation is to minimize airborne contaminants that can impair respiratory function and defense mechanisms [34,38,39,58]. Significant airborne contaminants include ammonia, hydrogen sulfide, carbon dioxide, carbon monoxide, methane, dust particles, and endotoxin. Ammonia and hydrogen sulfide are toxic gases and can contribute to respiratory damage, decreased mucociliary clearance, decreased alveolar macrophage activity, and overall compromise to respiratory defense mechanisms. Carbon dioxide, carbon monoxide, and methane contribute primarily as asphyxiative gases and generally do not contribute to significant impairment of the respiratory tract.

Dust particles also contribute to the impairment of respiratory defense mechanisms. Dust particles can arise from both organic and inorganic sources. In general, particles greater than 5 μm are filtered out by the nasal passages; most particles from 2 to 5 μm are removed by the mucociliary clearance of the trachea and bronchi, and particles less than 2 μm can penetrate to the alveolar spaces [47,58]. Organic and inorganic dust particles can impair mucociliary clearance and overload alveolar macrophage phagocytic clearance [58]. Organic dust particles are generally of more concern in confinement and intensive housing situations. In animal housing environments, most of the organic dust arises from fecal material, skin, and hair. Organic dust is significant in that it often contains high endotoxin and pathogen levels [38,39]. Inhaled endotoxin can contribute to pulmonary compromise by initiating inflammatory reactions within the alveoli and alveolar vascular endothelium.

Appropriate ventilation is also important in maintaining acceptable humidity and ambient temperature levels within confinement or semi-open housing. Observed thermoneutral ranges (the range of air temperature that sustains optimal performance) for a variety of domestic livestock are available (Table 1) [58]. In general, livestock can perform adequately within a fairly wide thermoneutral range. Higher temperatures, especially when combined with high humidity, tend to be more problematic than low temperatures [34]. Depending on the given climate and temperature ranges of a geographic region, housing ventilation will need to be designed to provide either heating or cooling or both. Cold temperatures and perhaps temperature fluctuations can decrease mucociliary clearance and predispose animals to respiratory disease [17]. Often, wide temperature fluctuations are more detrimental to animal health because they do not allow suitable adaptation over time.

There is minimal information on how ambient temperature directly relates to airborne pathogen biosecurity. Increased ambient temperature results in increased respiration and may increase pathogen shedding from infected animals. The direct effects of ambient temperature on pathogen survival are relatively unknown. Some studies suggest that the concentration of airborne particles is increased at low temperatures, and airborne bacterial concentrations were higher in winter than in summer [47].

There is slightly more information concerning the effects of relative humidity on pathogen survival and thus, airborne biosecurity [47,58]. In general, viruses with a hydrophobic lipid outer shell (i.e., enveloped viruses) survive better in lower humidity, and lipid-free viruses (i.e., foot-and-mouth disease virus) are more stable in moist air [18,47]. The four primary viral respiratory pathogens in cattle (bovine herpsevirus 1, bovine parainfluenza virus type 3, bovine respiratory syncytial virus, and bovine viral diarrhea virus) are all enveloped viruses and would be considered more stable in dry air, although

Table 1
Estimated thermoneutral values (°C) for several livestock species and age groups

Livestock group	Minimum acclimated temperature	Minimum ideal temperature	Maximum ideal temperature	Maximum acclimated temperature
Newborn calf	10	10	25	37
1-month-old calf	0	0	25	30
Veal calf	−15	−5	22	30
Beef cows	−17	−10	20	27
Dairy cow	−25	0	22	27
Ewe	−10	−5	25	37
Newborn lamb	20	20	32	37
Growing lamb	−12	0	22	37

From Wathes CM, Jones CD, Webster AJ. Ventilation, air hygiene and animal health. Vet Rec 1983;113:554–9; with permission.

the authors are unaware of specific studies documenting this conclusion. Gram-negative bacteria have outer phospholipid membranes and are also expected to be more stable in dry air [47]. *Mycoplasma* are reported to be sensitive to relative humidity between 40% and 70% [58]. Extrapolation of these limited data suggests that typical airborne pathogens associated with respiratory disease in domestic animals survive better in cool, dry air such as is observed in the late fall, winter, and early spring months. Although this correlates with clinical observations concerning the relative seasonal incidence of respiratory disease, a direct association has not been established. In beef cattle, seasonal increases in respiratory disease also correlate with seasonal management practices associated with movement of cattle to feedlots and increased animal density. It is likely that climate and management factors act together to dramatically increase pathogen exposure and transmission in feedlots. Alternatively, the high humidity that can be observed with dairy confinement housing in cold weather probably contributes to increased respiratory disease because of the higher pathogen density associated with increased aerosolized particle concentrations.

Ventilation systems should be constructed to provide even airflow throughout the structure without areas of air stagnation or drafts. Pockets of air stagnation have higher levels of airborne contaminants and contribute to the exposure and transmission of respiratory pathogens. Air stagnation can often be remedied by appropriate use of inexpensive fans. Correcting draft conditions can be more problematic and often requires complete evaluation of the housing structure for air leaks and evaluation of the ventilation system, especially air intake vents.

Guidelines for housing of livestock have been reported, including recommendations for ventilation (Table 2) [2,5,13,27,34,51,58]. Appropriate ventilation should flow from younger to older animals to minimize spread of pathogens to the more susceptible animals. The total air volume should be completely changed 4 times per hour in winter, and it should be changed up to 30 times per hour in summer [5,51]. The ventilation system should

Table 2
Recommended space requirements for calves

	Confinement housing				
Age of calf (wk)	<6	6–12	12–16		
Air volume (m^3/calf)	6	10	15		
	Open housing				
Age of calf (mo)	0–5	5–8	9–12	13–15	16–24
Sheltered area (ft^2/calf)	21	25	28	32	40
Outside open area (ft^2/calf)	30	35	40	45	50
Total area (ft^2/calf)	51	60	68	77	90

Confinement housing *From* Klingborg DJ. Preventing calf pneumonia. Compend Contin Educ Pract Vet 1986;8:F112–14; with permission.

Fundamental recommendations for ventilation systems in confinement and open-sheltered housing

Confinement housing

- Minimum of four air changes per hour (winter)
- Total exhaust capacity for up to 30 air changes per hour (summer)
- Continuous (not intermittent) ventilation
- Single-speed fans, not variable-speed fans, should be used
- Fans must be able to sustain 1/8-inch static pressure
- One must allow for two to four different ventilation rates using multiple fans
- Enough inlet slot area should be provided to allow minimal inlet velocity of 100 fpm (winter) and 800 fpm (summer)
- Thermostats should be used to control ventilation fans
- Thermostats should be located at eye level near the center of the barn
- The ventilation rate should be altered by stepping up the number of fans used for each level
- Wall fans should be mounted near the ceiling but collect air using ducts from within 38 cm (15 in) of the floor
- The fresh air intake should be located near the ceiling but at least 4 feet from any exhaust fan
- Adjustable eave slot inlets should be used to distribute incoming air uniformly
- A system for supplemental heat in the winter should be provided

Open-shelter housing

- Ventilation occurs through both open sides and the roof (ridge ventilation)
- Fully closed ends should be no more than 30 feet wide
- End widths greater than 30 feet require inlet ventilation
- Widths of 60 to 70 feet result in pockets of air stagnation
- The building should be oriented with the long axis perpendicular to the prevailing wind
- Open sides should face away from the prevailing wind
- Ventilation fans should be directed out of the downwind side of the building
- The building should be located upwind of other structures that might block air flow
- One should avoid placing shelter within 75 feet of other existing shelters or other obstructions

Data from Refs. [2,5,13,34,51].

provide constant rather than intermittent airflow. In the winter, the goal of ventilation is to minimize airborne pathogen density, remove excess moisture from animal respiration, and maintain adequate ambient temperature (10–13°C, 50–55°F). Although higher ventilation rates improve air quality, they are inefficient because they require excessive heating costs. Supplemental heating may be necessary as the outside temperature falls or stocking density decreases. At optimal stocking densities, livestock generally produce enough animal heat to maintain adequate ambient temperature in confined housing when outside temperatures remain above −8°C [51]. Winter ventilation is a compromise between the removal of airborne contaminants and the maintenance of ambient temperature. The primary goal of summer ventilation is to minimize ambient temperature and relative humidity. This requires high ventilation flow rates, which also enhance air quality. The goal is to maintain an ambient housing temperature to no more than 2°C above the outside temperature [5,51].

Relative humidity levels should be maintained between 50% and 80%, and ammonia levels should not exceed 10 ppm [2,34,47,51,58]. Maximum recommended stocking densities should not be exceeded (see Table 2) [26]. Separate age groups of cattle should be maintained in separate barns or be separated by barrier walls. Calf hutches for individual dairy calves provide an ideal means of managing relative calf isolation and limiting airborne transmission if they are properly positioned and spaced. Recommendations for calf hutches include one calf per hutch with a minimum separation of 4 feet between hutches. Hutches should be placed at least 10 feet from older-cattle enclosures and 50 feet from livestock building exhaust fans.

Commingling and animal contact

Many cattle management systems provide numerous opportunities for exchange of respiratory pathogens from animal to animal. Assembling groups of beef calves for a feedlot often involves mixing calves from different origins, congregation of animals at sale barns or other holding pens, and movement in congested cattle transports. These activities are well known to increase the rate of respiratory disease occurrence by stressing the animals and providing circumstances that decrease disease resistance. These same animal contact and crowding circumstances can dramatically increase exposure to pathogens, often including pathogens to which the animal has not developed prior immunity.

In a recent national survey, more than 50% of dairy producers housed sick animals in a manner that allowed direct nose-to-nose contact with healthy herdmates [54]. Many dairy producers expand their herds by purchasing animals from other sources, but less than 25% of them provide any quarantine time for the incoming animals. For producers who introduced 15% or more of their total animal inventory during an expansion, 16.6% reported an increase in occurrence of respiratory disease during the year [55].

During the early phases of respiratory disease, the shedding rates of pathogens via respiratory secretions increases dramatically. Commingling, crowding, and the animal stresses that are involved in animal movement can precipitate respiratory problems. These same factors can increase spread of pathogens to other animals with close contact. Although quarantine may not be effective against diseases with chronic carrier states such as Johne's disease, it can substantially decrease the risk of spreading respiratory pathogens. Furthermore, the duration of respiratory pathogen shedding has also been well characterized. In general, nasal shedding of viral respiratory pathogens is significantly reduced by 14 days after infection but may persist longer in individual animals, which suggests that quarantine for approximately 14 to 21 days should significantly reduce the exposure and transmission of these pathogens within an operation. Practical suggestions for limiting pathogen spread by contact include quarantine of incoming livestock, maintenance of hospital areas that do not allow contact with healthy animals, prevention of animal contact between different age groups of cattle, minimizing the time animals spend in market channels, and limiting the introduction of new animals to assembled herds or pens of cattle.

The concepts of pathogen transmission within grouped housing can be effectively applied to weaned dairy calves. Calves receive relatively low pathogen exposure while in calf hutches. On weaning and grouping in calf pens, the risk of exposure increases dramatically. It is important to appreciate that the risk of exposure rises with the number of calves housed together. For example, if one estimates that 5% of calves born in a herd with bovine viral diarrhea virus are persistently infected, then the probability of bovine viral diarrhea virus exposure in a group of 10 calves is approximately 0.4 ($1–0.95^{10}$). If the stocking rate increases to 30 calves, the probability nearly doubles to 0.78 ($1–0.95^{30}$). Limiting the number of calves per pen to less than seven is associated with decreased respiratory disease mortality [28] (also see article by Smith in this issue).

It must be emphasized that one animal can expose an entire pen of animals by simple close contact, airborne transmission, or environmental transmission at common housing areas such as feed bunks and water troughs. By dividing animals into smaller groups, the number of animals exposed is lowered significantly. Using the same example of bovine viral diarrhea virus exposure, if one splits the 30 calves into three separate pens, the probability of having all 30 calves exposed to bovine viral diarrhea virus falls from 0.78 to the comparatively negligible level of 0.064 [$(1–0.95^{10})^3$]. Simple segregation of animals is not sufficient unless physical barriers for fence line contact, separation of food and water troughs, segregation of likely fomites, and blocking airborne spread are used. These same principles can be applied to any group-housing situation. Such management and housing decisions must be made based on a balance between the risk and cost of disease versus the availability and cost of facilities and labor.

Minimizing the role of bovine viral diarrhea virus in bovine respiratory disease

It was noted previously that the common bovine respiratory pathogens are considered to be ubiquitous in cattle populations in the United States and most other countries. Although this does not suggest that every animal harbors each pathogen, these agents can be found routinely in the nasopharynx of healthy and diseased animals within most herds. In contrast, some European countries have successfully eradicated some viral respiratory pathogens such as bovine herpesvirus 1 and bovine viral diarrhea virus (BVDV) from cattle populations. Under the currently prevailing practices within the United States and many other countries, the authors do not suggest testing or identification of most respiratory pathogens as a viable means to identify carriers or to exclude the animals from introduction into a herd. The exception to this is BVDV. Although BVDV is not considered a primary pneumopathogen, it is considered to have an important role in respiratory disease of cattle [2,41]. The immunosuppressive effects of the virus and the close association of BVDV infection and respiratory disease occurrence in some epidemiologic studies suggest that the virus plays a role by promoting secondary bacterial lung infection.

Although BVDV vaccines have been improved over the past several years, vaccination alone rarely eliminates BVDV from an infected herd. An effective BVDV biosecurity program must include the identification and removal of persistently infected animals, BVDV screening of incoming animals and their calves, and a comprehensive vaccination program [7,8,25,57]. Persistently infected cattle do not mount an effective immune response against the virus and are capable of shedding large amounts of the virus into the environment through multiple routes. Persistently infected animals have been implicated as the primary means by which BVDV infection is maintained in assembled dairy herds, and they are also considered a significant threat for transmission in cow–calf and feedlot operations [20–23,32,50,60]. With the development of new tests over the past several years, our ability to accurately and expediently identify persistently infected animals has dramatically improved [9,25]. The serum immunoperoxidase monolayer assay (IPMA) and antigen capture ELISA tests and the immunohistochemistry test of skin biopsy material have appropriate sensitivity and specificity for detecting persistently infected cattle.

The authors do not know of significant published research that evaluates the effect of test-and-cull strategies for BVDV on the occurrence of BRDC; however, elimination of persistently infected animals from herds can have significant positive effects in decreasing other BVDV manifestations such as reproductive failure. Implementing test-and-cull procedures for persistently infected animals may prove to be a powerful means of decreasing BRDC prevalence.

In general, all cattle introduced into a herd should be tested for BVDV before purchase or entry. Acute BVDV infections of pregnant cattle can result in animals that are BVDV negative at the time of testing while the fetus is persistently infected. It is critical that all calves from newly introduced pregnant animals also be tested immediately after birth. To establish a BVDV-negative herd, it is generally more effective and economical to test calves as they are born rather than screen adult populations. A negative result for a calf indicates that not only the calf but also all of the calf's maternal ancestors are not persistently infected. A single positive test on a calf does not differentiate between acute and persistent infection. A confirmatory test may be performed in 4 weeks, or the animal may be assumed to be persistently infected and euthanized or sold for slaughter. The dams of all persistently infected calves should be traced and tested as well to determine their status. In most cases, these animals will test negative, indicating fetal exposure due to acute infection during gestation. Bulls should also be tested because they can contribute to animal exposure within a herd.

Summary

Although biosecurity practices play a role in minimizing respiratory disease in cattle, they must be used in combination with other management strategies that address the many other risk factors. Because the pathogens involved in bovine respiratory disease are enzootic in the general cattle population, biosecurity practices aimed at the complete elimination of exposure are currently impractical. Several animal husbandry and production management practices can be used to minimize pathogen shedding, exposure, and transmission within a given population, however. Various combinations of these control measures can be applied to individual farms to help decrease the morbidity and mortality attributed to respiratory disease.

References

[1] Ames TR. Dairy calf pneumonia: the disease and its impact. Vet Clin North Am Food Anim Pract 1997;13:379–91.
[2] Ames TR, Baker JC, Wikse SE. The bronchopneumonias (respiratory disease complex of cattle, sheep, and goats). In: Smith BP, editor. Large animal internal medicine, 3rd edition. St. Louis: Mosby; 2002. p. 551–70.
[3] Anderson JF, Bates DW. Appraising the adequacy of environment for confined animals. Vet Med Small Anim Clin 1979;74:208–10.
[4] Anderson JF, Bates DW. Influence of improved ventilation on health of confined cattle. J Am Vet Med Assoc 1979;174:577–80.
[5] Bates DW, Anderson JF. Calculation of ventilation needs for confined cattle. J Am Vet Med Assoc 1979;174:581–9.
[6] Beer M, Hehnen HR, Wolfmeyer A, et al. A new inactivated BVDV genotype I and II vaccine: an immunisation and challenge study with BVDV genotype I. Vet Microbiol 2000;77:195–208.

[7] Bitsch V, Ronsholt L. Control of bovine viral diarrhea virus infection without vaccines. Vet Clin North Am Food Anim Pract 1995;11:627–40.
[8] Bolin SR. Control of bovine viral diarrhea infection by use of vaccination. Vet Clin North Am Food Anim Pract 1995;11:615–25.
[9] Brock KV. Diagnosis of bovine viral diarrhea virus infections. Vet Clin North Am Food Anim Pract 1995;11:549–61.
[10] Christensen LS, Mortensen S, Botner A, et al. Further evidence of long distance airborne transmission of Aujeszky's disease (pseudorabies) virus. Vet Rec 1993;132:317–21.
[11] Christensen LS, Mousing J, Mortensen S, et al. Evidence of long distance airborne transmission of Aujeszky's disease (pseudorabies) virus. Vet Rec 1990;127:471–4.
[12] Cole NA. Preconditioning calves for the feedlot. Vet Clin North Am Food Anim Pract 1985;1:401–11.
[13] Collins Jr. ER. Ventilation of sheep and goat barns. Vet Clin North Am Food Anim Pract 1990;6:635–54.
[14] Curtis SE. Air environment and animal performance. J Anim Sci 1972;35:628–34.
[15] Daggupaty SM, Sellers RF. Airborne spread of foot-and-mouth disease in Saskatchewan. Canada, 1951–1952. Can J Vet Res 1990;54:465–8.
[16] Dean HJ, Leyh R. Cross-protective efficacy of a bovine viral diarrhea virus (BVDV) type 1 vaccine against BVDV type 2 challenge. Vaccine 1999;17:1117–24.
[17] Diesel DA, Lebel JL, Tucker A. Pulmonary particle deposition and airway mucociliary clearance in cold-exposed calves. Am J Vet Res 1991;52:1665–71.
[18] Donaldson AI. Factors influencing the dispersal, survival and deposition of airborne pathogens of farm animals. Vet Bull 1978;48:83–94.
[19] 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.
[20] Houe H. Age distribution of animals persistently infected with bovine virus diarrhea virus in twenty-two Danish dairy herds. Can J Vet Res 1992;56:194–8.
[21] Houe H. Epidemiological features and economical importance of bovine virus diarrhoea virus (BVDV) infections. Vet Microbiol 1999;64:89–107.
[22] Houe H. Epidemiology of bovine viral diarrhea virus. Vet Clin North Am Food Anim Pract 1995;11:521–47.
[23] Houe H, Baker JC, Maes RK, et al. Prevalence of cattle persistently infected with bovine viral diarrhea virus in 20 dairy herds in two counties in central Michigan and comparison of prevalence of antibody-positive cattle among herds with different infection and vaccination status. J Vet Diagn Invest 1995;7:321–6.
[24] Hum S, Kessell A, Djordjevic S, et al. Mastitis, polyarthritis and abortion caused by Mycoplasma species bovine group 7 in dairy cattle. Aust Vet J 2000;78:744–50.
[25] Kelling CL, Grotelueschen DM, Smith DR, et al. Testing and management strategies for effective beef and dairy herd BVDV biosecurity programs. The Bovine Practitioner 2000;34: 13–22.
[26] Klingborg DJ. Preventing calf pneumonia. Compend Contin Educ Pract Vet 1986;8: F112–4.
[27] Linklater KA, Watson GA. Sheep housing and health. Vet Rec 1983;113:560–4.
[28] Losinger WC, 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.
[29] Mars MH, Bruschke CJ, van Oirschot JT. Airborne transmission of BHV1. BRSV, and BVDV among cattle is possible under experimental conditions. Vet Microbiol 1999;66: 197–207.
[30] Mars MH, de Jong MC, van Maanen C, et al. Airborne transmission of bovine herpesvirus 1 infections in calves under field conditions. Vet Microbiol 2000;76:1–3.
[31] Meyer VM. Ventilation systems for swine housing. Vet Med Small Anim Clin 1975;70: 992–3.

[32] Moerman A, Straver PJ, de Jong MC, et al. A long term epidemiological study of bovine viral diarrhoea infections in a large herd of dairy cattle. Vet Rec 1993;132:622–6.
[33] 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.
[34] Parker WH. Housing of ruminants: II. requirements of good housing and effects of bad housing. Vet Rec 1968;83:364–8.
[35] Perino LJ. Advances in pulmonary immunology. Vet Clin North Am Food Anim Pract 1997;13:393–9.
[36] Perino, LJ, Wittum, TE, Ross, GS, et al. Failure of passive transfer: risk factors and effects on lifetime performance. In: Proceedings of the American Association of Bovine Practitioners, 28th Annual AABP Convention. San Antonio (TX); 1996. p. 101–10.
[37] Pfutzner H, Sachse K. *Mycoplasma bovis* as an agent of mastitis, pneumonia, arthritis and genital disorders in cattle. Rev Sci Tech 1996;15:1477–94.
[38] Pickrell J. Hazards in confinement housing—gases and dusts in confined animal houses for swine, poultry, horses and humans. Vet Hum Toxicol 1991;33:32–9.
[39] Pickrell JA, Heber AJ, Murphy JP, et al. Characterization of particles, ammonia and endotoxin in swine confinement operations. Vet Hum Toxicol 1993;35:421–8.
[40] Pierson RE, Kainer RA. Clinical classification of pneumonias in cattle. The Bovine Practitioner 1980;15:73–9.
[41] Potgieter LN. Bovine respiratory tract disease caused by bovine viral diarrhea virus. Vet Clin North Am Food Anim Pract 1997;13:471–81.
[42] Ribble CS. Assessing vaccine efficacy. Can Vet J 1990;31:679–81.
[43] Sainsbury DW. Housing of livestock: II. practical considerations of ventilation and construction. Veterinarian 1966;4:29–32.
[44] 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.
[45] Sorensen JH, Mackay DK, Jensen CO, et al. An integrated model to predict the atmospheric spread of foot-and-mouth disease virus. Epidemiol Infect 2000;124:577–90.
[46] Speer NC, Young C, Roeber D. The importance of preventing bovine respiratory disease: A beef industry review. The Bovine Practitioner 2001;35:189–96.
[47] Stark KD. The role of infectious aerosols in disease transmission in pigs. Vet J 1999;158: 164–81.
[48] Step DL. Mycoplasma infection in cattle: I pneumonia-arthritis syndrome. The Bovine Practitioner 2001;35:149–55.
[49] Stipkovits L, Ripley P, Varga J, et al. Clinical study of the disease of calves associated with *Mycoplasma bovis* infection. Acta Vet Hung 2000;48:387–95.
[50] Taylor LF, Van Donkersgoed J, Dubovi EJ, et al. The prevalence of bovine viral diarrhea virus infection in a population of feedlot calves in western Canada. Can J Vet Res 1995;59:87–93.
[51] Turnbull JE. Housing and environment for dairy calves. Can Vet J 1980;21:85–90.
[52] USDA. APHIS:VS Centers for Epidemiology and Animal Health NAHMS. Beef '97, part II: reference of 1997 beef cow-calf health & health management practices, 1997, Report #N238.797.
[53] USDA. APHIS:VS Centers for Epidemiology and Animal Health NAHMS. Cattle and calves death loss, 1995, Report #N232.397.
[54] USDA. APHIS:VS Centers for Epidemiology and Animal Health NAHMS. Dairy '96, part I: reference of 1996 dairy management practices, 1996, Report #N200.696.
[55] USDA. APHIS:VS Centers for Epidemiology and Animal Health NAHMS. Dairy '96, part III: reference of 1996 dairy health and health management, 1996, Report #N212.1196.
[56] USDA. APHIS:VS Centers for Epidemiology and Animal Health NAHMS. Feedlot '99, part III: health management and biosecurity in U.S. feedlots, 2000, Report #N336.1200.
[57] Van Oirschot JT, Bruschke CJ, van Rijn PA. Vaccination of cattle against bovine viral diarrhoea. Vet Microbiol 1999;64:169–83.

[58] Wathes CM, Jones CD, Webster AJ. Ventilation, air hygiene and animal health. Vet Rec 1983;113:554–9.
[59] West K, Petrie L, Konoby C, et al. The efficacy of modified-live bovine respiratory syncytial virus vaccines in experimentally infected calves. Vaccine 1999;18:907–19.
[60] Wittum TE, Grotelueschen DM, Brock KV, et al. Persistent bovine viral diarrhoea virus infection in US beef herds. Prev Vet Med 2001;49:83–94.