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Prevention of Respiratory Disease in Cow/Calf Operations

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KEYWORDS

• Respiratory disease • Cow • Calf • Risk factors

Respiratory disease of calves from birth until weaning in cow/calf operations is common, yet sporadic in occurrence and usually with low prevalence. Dewell and colleagues[1] reported a 12% overall morbidity in a group of 1556 calves, of which 39% (4.7% case specific) was due to respiratory disease. In a survey of 520 cow/calf producers in Canada the incidence of preweaning mortality (5.4%–5.6%) attributed to pneumonia ranges from 12.8% to 17.5%, with greater losses occurring on larger operations.[2] The diagnosis of pneumonia in calves between the age of 1 month and weaning is generally termed nursing calf pneumonia, or in the case of spring calving herds, summer pneumonia. Although the common risk factors associated with bovine respiratory disease (BRD) in postweaned calves, such as commingling, transportation stress, and dietary changes, can be identified in cases of nursing calf pneumonia, they may not be of primary importance.

RISK FACTORS

Identification of risk factors associated with calf pneumonia in beef herds is an important step in attempts to manage this disease. An acceptable way to consider and quantify the causative factors with clinical disease is in the form of a logistic regression equation. This type of equation represents the relationship between the probability of disease and the presence or absence of one or more risk factors.[3–6] Risk factors associated with a clinical disease (ie, nursing calf pneumonia) should include

1. Failure or partial failure of passive transfer
2. Any type of commingling of different groups, even those belonging to the same operation, such as in extended calving intervals or 2 different calving seasons
3. Environmental risk, extreme cold or heat along with precipitation
4. Nutritional risk, such as a change in diet, energy, and protein deficiency

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5. Exposure to pathogens such as bovine herpesvirus 1 (BHV-1), bovine virus diarrhea virus (BVDV), bovine respiratory syncytial virus (BRSV), bovine respiratory coronavirus (BRCV), and *Mycoplasma bovis*
6. Trace mineral deficiency
7. Handling stress
8. Other operation-specific risk factors.

Each one of these risk factors or a combination of several can result in enough stress to allow clinical disease to manifest itself. A regression equation Y = b0 + b1X1 + b2X2 + … + bkXk, for respiratory disease may resemble this model: Y = 0.2 + 0.2(X1) + 0.1(X2) + 0.1(X3) + 0.15(X4) + …., where Y is the probability of respiratory disease, X1 is the degree of failure of passive transfer, X2 is the nutritional status of the cow and newborn calf, X3 is environmental influences such as rain or snow and cold temperatures, and X4 is exposure to pathogens. Although this approach helps to provide an understanding of the risk factors and explain the cause of the disease, the diagnostic ability to identify or even influence some of these factors is not always apparent. Producers can become frustrated with control programs that focus on only 1 or 2 factors. In herd investigations each risk factor must be considered.

EFFECT OF MATERNAL IMMUNITY

The role of maternal immunity and its relationship to health in calves is clear. Its role as a risk factor with respiratory disease in nursing calves is not so clearly defined. Wittum and Perino[7] showed that calves with failure of passive transfer were 3.2 to 9.5 times more likely to become sick and 5.4 times more likely to die before weaning than calves with normal passive transfer. Faber and colleagues[8] reported on the role of passive transfer in reducing risk of illness and mortality and on lifetime effects in dairy cattle. Dewell and colleagues[1] reported that calves with serum IgG concentrations of at least 2700 mg/dL weighed an estimated 3.34 kg (7.38 pounds) more at 205 days of age than calves with lower serum IgG concentration. The effect on performance was also noted in lambs, in which there was a significant association with IgG concentration at 24 hours of age and mean daily gain.[9] The research makes it clear that a partial or complete failure of passive transfer is one of the most important risk factors leading to the development of clinical disease and a negative effect on performance. How does maternal immunity play a role in preventing clinical disease in neonatal and young calves? In the bovine, with syndesmochorial placentation, transfer of immunity does not take place during gestation. Although the fetus is able to mount an active immune response during gestation, the newborn is essentially lacking protection against common organisms that in the adult cause no clinical disease.[10] Other immune factors also seem to play a role in disease protection and production performance in the young bovine.

Antibodies, Cytokines, and Maternal Cell Transfer

Disease protection for the newborn is conferred by the transfer of antibody, primarily through the absorption of IgG1. All classes of immunoglobulins IgG, IgM, and IgA are absorbed, with IgA and IgG1 being resecreted to provide mucosal protection. In addition to immunoglobulins, other immune-protective components are part of passive transfer.

Hirako and colleagues[11] showed that proinflammatory immune cytokines interleukin 1β (IL1β), IL1 receptor antagonist, and tumor necrosis factor α (TNF-α) were lower in postcolostrum-fed calves that became clinically ill in the first 4 months of life. Proinflammatory cytokines are necessary to activate innate and active immunity.

Lymphocytes from the dam are passed to the neonate via the colostrum. These lymphocytes may survive for a period of time in the intestinal lumen but may also penetrate the mucosa and find residence in the mesenteric lymph nodes. This transfer may allow for cell-mediated immunity to be passed to the newborn from the dam. Archambault and colleagues[12] reported that cell-mediated immune transfer to neonates could be enhanced by maternal vaccination. Although Donovan and colleagues[13] showed that transfer of live maternal cells from colostrum to neonatal calves enhanced responses to antigens against which the dams had previously responded (BVDV), but not to antigens to which the dams were naive, our complete understanding of the role of lymphocyte transfer is still not clear. What is clear is there is no true substitute for the passage of maternal immunity from dam to the neonate. Colostral supplements, substitutes, and frozen colostrum, although valuable as an addition to fresh colostrum, cannot match the quality of the dam's fresh colostrum.[14]

Quality, Concentration, and Volume

Measurement of maternal immunity is centered on the measurement of the amount of immunoglobulins in the bloodstream. Measurement of total proteins with the refractometer can give a qualitative measurement of passive transfer.[15] Total proteins in the serum that are equal to or greater than 5.5 provide a yes or no answer to whether passive transfer has occurred. Dewell and colleagues[1] showed that quantitative differences in passive transfer may result in differences in outcomes of disease and performance. Calves with serum IgG1 levels up to 2500 mg/dL were 1.5 times more likely to get sick before weaning and 2.4 times more likely to die before weaning than calves with higher IgG1 levels. Calves need to acquire as much protection as possible from the dam's colostrum. Anything less than maximum absorption seems to increase health and performance risk.

Absorption

The volume intake of colostrum is positively correlated with passive transfer, but how does adequate transfer occur in beef cattle with at times a very low volume of colostrum? In a Canadian study, colostrum production in beef cows ranged from 0.9 to 5 L. In the same study the production of colostral immunoglobulins ranged from 103 to 525 g.[16] If the requirement of the calf to achieve adequate transfer is 300 g, then with a concentration of 150 g/L, the neonate would need to consume 2 L at an efficiency of absorption at 100%. Estimates of absorption range from 6% to 88%, although most estimates fall in the range of 20% to 35%.[17,18] If one assumes an efficiency of absorption of 35% and a colostral concentration value of 100 g/L, then to achieve a serum concentration of 20 g/L, with a total serum volume of 4 L (serum volume 59.6% of body weight), the calf would have to consume approximately 2.3 L.

$$\text{Consumption in grams of Ig's } (100 \times 2.3 \text{ L}) \times \%\text{AEA/plasma volume}$$
$$(\text{Body weight} \times 9.6\%)\ (0.35/4\text{L}) = \text{expected Ig concentration } 20.125 \text{ g/L}$$

With this knowledge it becomes imperative that any investigation of respiratory disease in suckling calves must begin with an analysis of factors that influence the passage of immunity from dam to calf.

GENETIC RISK

Calving ease is an important genetic trait that affects passive transfer via stress level at birth. Besser and colleagues[19] reported that calves experiencing dystocia had lower absorption of IgG1 from colostrum associated with respiratory acidosis. Calves

born after experiencing calving difficulty have a physiologic acidosis. In addition, increased calving difficulty is associated with extended time to nursing.[20] Because time to first nursing is associated with efficiency of absorption, this too is a factor related to efficiency of passive transfer. It is important to recognize the role of calving ease in the equation of long-term health of calves. A second genetic trait associated with passive transfer is that of udder and teat conformation. The mechanics of transfer are critical to passive transfer, that is, teat size and length, and udder attachment. Goonewardene and colleagues[21] reported that pendulous udders coupled with large teat size can complicate the suckling process. This situation reduces the probability of good immune transfer, which increases the risk of clinical disease and decrease growth rates. A third genetic trait is the selection for increased growth rates in calves. Muggli and colleagues[22] reported that calves from Hereford lines selected for performance had lower IgG1 concentration than calves from the randomly selected control line. Field observations seem to support this research observation. Herds with selection pressure exclusively on performance tend to experience a higher level of clinical disease, often in the form of respiratory disease. The reason for this may not be evident; however, it may seem logical that selection for performance also leads to an increase in birth weight, calving difficulty, longer period of time to standing and nursing, or perhaps greater milk production leading to a higher incidence of mastitis or udder and teat problems, thus leading to decreased absorption of immunity.

HANDLING RISK

Maternal stress is another risk factor that must be considered. Tuchscherer and colleagues[23] reported the effect of maternal stress in sows and its subsequent negative effect on passive transfer with the sequelae of higher morbidity and mortality in suckling pigs. Lay and colleagues[24] reported on stress in pregnant cows exposed to repeated transportation and the negative effect on the progeny to respond to stress. It is evident from these studies that repeated stress in the pregnant female can have a detrimental effect on the health of offspring. The application of this directly relates to adopting low-stress handling methods of pregnant females.

COMMINGLING RISK

Commingling risk in postweaned calves has been well documented to be a major risk factor in the development of BRD.[25–27] On the other hand, commingling stress is not usually a prime risk factor in respiratory disease of young calves. When calves are moved to new pastures during the grazing season or combined with different groups, or sorted during estrous synchronization procedures, this stressor can be involved. Thus, any investigation of respiratory disease in young calves must include this potential risk factor.

ENVIRONMENTAL RISK

Environmental risk is a third risk factor.[28] The stress of heat and humidity as described by the temperature humidity index has been associated with an increase in early embryonic loss in dairy cattle.[29] Environmental risk can affect transfer of maternal immunity. Calves born in extremely harsh environmental conditions such as cold or heat have delayed time to nursing, and the stress associated with controlling homeostasis. Carstens[30] states calf mortality increases with decreases in ambient temperature or when precipitation occurs on the day of birth.

NUTRITIONAL RISK

Nutritional restriction of energy and protein in the beef cow can have profound effects on the developing fetus. Long and colleagues[31] showed that restriction of the cow resulted in a decrease in placentation area. Larson and colleagues[32] reported an increase in calf weaning weight from cows on winter range receiving adequate protein supplementation in late gestation versus cows on restricted protein diets. Late gestation protein supplementation of cows also improved carcass quality in steers born to protein-supplemented cows. These effects are analogous to the detrimental effects of nutritional restriction in gestating sows on fetal myogenesis, birth weight, and postnatal growth.[33] Odde[20] reported that body condition score (BCS) influenced time to standing for a newborn calf. Calves born to cows with BCS 4 took approximately 60 minutes to stand in contrast to calves born to cows with BCS 5, which took 43 minutes to stand. Time to standing has a direct influence on intake and absorption of colostral immune factors.

PATHOGEN RISK

The most common approach when dealing with respiratory outbreaks in suckling calves is to identify the most likely viral and/or bacterial pathogens as the cause. Although this is an important part of prevention and treatment strategies, the cause may be more symptomatic rather than a major risk factor, particularly as it applies to secondary bacterial pathogens. Most cow/calf herds are maintained in multiple pasture units on a single operation. Exposure within these units to potential pathogens is common. In many herds, pathogens such as BRSV have likely become endemic and are not likely to cause significant clinical disease in well-vaccinated herds. In herd situations with exposure to BVDV persistent infection (PI) animals in the absence of other risk factors may result in clinical disease.[34] Exposure to cattle from other operations may present a pathogen risk because naive cattle exposed to the common viral pathogens such as infectious bovine rhinotracheitis (IBR), BRSV, BVDV, and BRCV as well as the bacterial pathogen such as *Mycoplasma bovis*[35,36] may cause clinical disease in the absence of other apparent risk factors. The risk posed by these viral pathogens is readily reduced by herd vaccination programs. The use of modified live virus (MLV) vaccines greatly decreases shedding of these viruses and reduces the risk of clinical disease. The pathogen previously characterized as *Pasteurella trehalosi* and recently renamed *Bibersteinia trehalosi* has long been recognized as a cause of ovine respiratory disease in small ruminants.[37,38] Its role in acute cases of respiratory disease in young dairy and stocker calves seems to be increasing and may be influenced by the use of prophylactic antibiotics given to control other pathogens.[39] Vaccination to control bacterial pathogens gives mixed results in the field. This finding could be due to timing of vaccination, not given before pathogen exposure, lack of booster doses, and lack of attention to the primary causative risk factors.

COST OF ILLNESS

The cost of respiratory disease in nursing calves is not easily measurable, therefore some assumptions must be made. Weaning weights are generally assumed to be less with any clinical disease such as calf scours. With respiratory disease the assumption is that weaning weights are reduced by as much as 15.87 kg (35 pounds) on average.[7] This loss does not include treatment costs or time and labor associated with treatment or death loss. If the value of gain at the calf level until weaning is approximately $1.10/kg ($0.50/pound), then a loss of weaning weight of 15.87 kg (35 pounds) would be worth $17.50. If treatment costs including labor are $20/calf,

and assuming no death loss, then the cost of one calf needing treatment would be $37.50. If the percentage of calves becoming ill during the suckling phase is 10%, then the cost of illness for each calf in the herd would be $3.75. When death loss occurs and is included in this calculation the cost of illness increases dramatically. If the value of each calf lost is equal to the cost of keeping a cow on an annual basis (eg, $500), then each 1% death loss increases the cost of respiratory disease for each surviving calf by $5.00/calf. Thus, if the percentage of calves needing treatment is 10% and death loss is 1%, then the total cost of respiratory disease would be $8.75 for each surviving calf. With proper herd health management, attention to common risk factors, and the use of specific vaccines most herd outbreaks of respiratory disease in suckling calves can be reduced or prevented.

MANAGEMENT OF RESPIRATORY DISEASE IN SUCKLING CALVES

Management of respiratory disease in suckling calves requires knowledge of all the risk factors contributing to the signs and symptoms of clinical disease. Signs and symptoms of respiratory disease in calves include increased respiratory rates, increased rectal temperature, a single or both ears drooped, and depression. It is difficult to distinguish the causative agents based on clinical signs. It is also likely that most cases of respiratory disease are the result of infections by multiple pathogens. For the veterinarian to manage and prevent these cases, it is necessary to logically create a list of risk factors most likely involved in the outbreak.

VACCINATION

Vaccination of young calves (30–60 days) to prevent respiratory disease has become a common management practice. Beef calves are commonly vaccinated against clostridial diseases at a young age. Although reports suggest that vaccination produces a limited antibody response in young calves,[40] this practice seems to be an effective management strategy as the prevalence of clostridial diseases such as blackleg, malignant edema, and gas gangrene become rare in vaccinated populations. The addition of viral vaccines and bacterins to prevent respiratory disease is also now commonly included. Their efficacy has come under some scrutiny as even in well-vaccinated herds cases of respiratory disease may still occur. Vaccines are given to prevent clinical disease and pathogen transmission caused by specific pathogens. IBR vaccine is given to prevent IBR. It is not possible to vaccinate against every pathogen known to cause respiratory disease. Nor do all vaccines provide equal levels of protection or efficacy. It becomes critical to prioritize vaccines given to young calves. To do this the veterinarian must have a guiding principle regarding vaccination. It is helpful to ask 3 questions:

1. Is there a substantial risk of disease caused by a specific pathogen?
2. Is there a commercial vaccine that has shown efficacy against the specific pathogen?
3. Does management of the herd allow for the proper use of the vaccine within the constraints of handling times?

If the answer is no to any of these questions, then it begs the questions, why recommend their use at all and will other risk management strategies prove to be as effective?

VACCINE INTERFERENCE

A common practice among cattle producers is to use combination vaccines, which combine several different antigens into a single injection. The advantage of this

approach is to reduce the number of injections given to animals yet achieve the same level of immunity as if each antigen had been given independently. Biologics manufacturers must prove to the United States Department of Agriculture that there is no interference among individual antigens when given together in a single dose. What is not well understood is the potential for interference when different vaccines are given concurrently. As was stated earlier, it is a common practice to give MLV vaccines along with bacterins. Studies have shown that vaccine interactions may occur when giving an MLV vaccine along with bacterins.[41] Immune interaction, defined by a diminished immune response to one or more of the antigens given concurrently, was recently reported in 2 separate trials.[42] This interaction seems to be confined to animals that are naive to the antigens given.

MATERNAL IMMUNITY AND VACCINATION

What is the role of maternal immunity on vaccination of the young calf? Does the presence of maternal antibody interfere with an active immune response? Woolums and Smith[43] reviewed and described reasons for lack of protection following vaccination in young calves: age of calf at vaccination, amount of maternal antibody, type of vaccine, virulence of the pathogen challenge, and the outcome that was used to describe the success or failure of the vaccination. With BHV-1, the antibody response in the presence of antibody is negligible; however, on receiving a second dose even months later the response was greater than calves receiving their initial dose at this same time.[44] In BVDV, the literature is less clearly defined.[45–47] What is clear is that calves without maternal immunity to BVDV can respond to MLV vaccine, whereas at higher levels of maternal antibody, antibody production is blocked and cell-mediated immune (CMI) responses are primed.[48] Vaccination of young calves with BRSV has shown a CMI response in the presence of maternal antibody.[49] In a recent study intranasal vaccination with BRSV showed protection against BRSV challenge as measured by virus shedding.[50] The data indicate that young beef calves can respond to vaccination, and response as measured by antibody production is affected in the presence of maternal immunity. A population of memory cells can be generated and when either vaccination or exposure occurs, immunization has provided a degree of protection not seen in nonvaccinated animals.

POPULATION DYNAMICS

Methods to control disease in beef cattle populations have traditionally been focused on immunization to prevent clinical disease. Whereas prevention of clinical disease is a direct effect of immunization, the indirect effect of disease prevention by decreasing transmission is of primary importance with pathogens that are transmitted from animal to animal.[51]

In human medical literature, the concept of population/herd immunity has successfully been used to implement vaccination programs designed to protect populations against specific pathogens. Specifically, they include diphtheria, tetanus, and pertussis, and also measles, mumps and rubella, as well as poliomyelitis.[52] Although we are concerned about each individual being protected against disease, the greater purpose is to immunize as many as possible within the population such that susceptible individuals within a population are also protected. A greater level of population protection can be achieved by

1. Reducing the number of animals shedding disease pathogens
2. Decreasing the amount of pathogens shed by infected animals

3. Decreasing the duration of shedding
4. Increasing the infectious dose necessary to cause infection.

The percentage of immune individuals in a population to achieve herd protection varies by pathogen, but ranges from 83% to 94%.[53] This concept is the basic premise of herd vaccination programs.

In the veterinary medicine community there is some debate about the practice of annual booster vaccinations in companion animals because some boosters may no longer be necessary for clinical disease prevention because of low risk.[54] For veterinarians in food animal practice there are questions as to efficacy, duration of immunity, and number of doses needed to achieve significant population and individual animal protection.[55,56] Veterinarians are called on to make recommendations concerning vaccination protocols for multiple diverse livestock businesses. To do so they require in-depth herd knowledge regarding some assessment of risk for specific diseases, management, genetics, nutrition status, and handling facilities. For example, in beef cattle breeding herds, purchased females or bulls may be introduced into new herds without benefit of a quarantine period, biosecurity testing, or knowledge of purchased animals' herd disease status. Even when vaccination programs are specifically outlined, it is rare for buyers to seek veterinary advice as to the quality of the program.

In IBR-vaccinated animals, protective immunity is assumed regardless of type of vaccine, with MLV vaccines providing better protection.[57] Although the issue of duration of immunity and protection may be debated, the real issue is one of risk analysis and risk management. What is the risk of the herd being exposed to a field challenge with either IBR or BVDV? In most commercial operations this risk exists, but is difficult to quantify. In most purchases this approach does not have negative consequences; however, in a quality control system with responsibility for disease control, the veterinarian will likely seek to lower the risk of exposure and increase specific immunity to the pathogens considered to be of greatest risk.

In most livestock businesses the risk of exposure to common pathogens is not known. However, there is information as to the number of immune animals necessary to prevent spread of disease. By using this information the veterinarian can make informed recommendations regarding the type of vaccine, the timing of boosters, and the frequency of vaccination. The spread of disease depends on the basic reproductive rate (R_o). The basic reproduction number R_o is the number of secondary infections resulting from one primary case in a totally susceptible population. The basic reproduction number is a feature of the infectious agent and the host population without a control measure being active.

If R_o in a vaccinated population is larger than 1, then the vaccine cannot totally prevent the spread of infection and additional biosecurity principles must be used.[58] It has been estimated that for BHV-1 infections R_o is approximately 7.0. After using 2 different vaccines it was estimated that R_o was 2.4 and 1.1.[59] This finding means that within a susceptible population, 2.4 or 1.1 new cases will arise from 1 case. In this immunized population transmission cannot effectively be prevented. Within real populations these numbers must be considered within the context that as animals become infected and are contagious, the number of susceptible animals declines and the number of recovered and immune animals increases. It has been estimated that the critical proportion of immune animals is expressed by the equation critical proportion $= 1 - 1/R_o$. The higher the R_o the greater the number of animals that must be immune to prevent spread of the infectious agent. If $R_o = 7.0$ for a specific pathogen, then the proportion of immune animals within that population must be $1 - (1/7)$. This calculation means that approximately 86% of the population must be

immune to prevent transmission. Estimates for limiting the spread of BVDV within a population have been made based on mathematical models. In herds without PI animals, 57% of the animals must be immune to stop transmission. For herds with animals that are persistently infected with BVDV, 97% must be immune.[60] This issue of herd immunity to BVDV is further complicated by the amount of cross-protection afforded by commercial vaccines, as strain differences can exist between vaccine virus and wild virus.[61] A sound recommendation for vaccines can be made based only on actual challenge model and field trials using sound science and proper design.

The challenge of making sound vaccination recommendations as part of an overall herd health program is the responsibility of food animal veterinarians. Making those recommendations requires an in-depth knowledge of the risk of disease, management ability, facilities, nutritional requirements, and in breeding herds the current genetic base. In addition, veterinarians must have a working knowledge of the relative efficacy, duration of immunity, and the effect on transmission of the available commercial vaccines. With this as a working tool, the veterinarian can use the concept of population dynamics and herd immunity when making specific herd recommendations regarding the timing and frequency of vaccination administration.[62]

SUMMARY

When investigating outbreaks of respiratory disease in young calves, it is important to review all of the risk factors that could potentially contribute to the clinical disease. A list of risk factors should include

1. Failure or partial failure of passive transfer. This may be due to
    - Cows in low body condition score
    - Udder and teat conformation
    - Genetic type, selection for moderate growth versus high performance (select for type based on resources available to the operation)
2. Genetic risk
    - Dystocia
    - Mothering ability
    - Udder and teat conformation
2. Any type of commingling of different groups, even those belonging to the same operation
    - Moving long distances to new pastures
    - Combining different pasture groups together before weaning
3. Environmental risk
    - Heat risk
    - Cold risk
    - Snow and freezing rain
4. Nutritional risk, such as a change in diet
    - Creep feeding
    - Lush pastures
    - Drought-stressed pastures
5. Exposure to pathogens such as IBR, BVDV, BRSV, BRCV, and *Mycoplasma bovis*
    - Within-herd exposure or exposure to other populations
6. Trace mineral deficiency or toxicity
    - Cu, Se, Zn
    - Sulfur
7. Other risk factors
    - Lack of adequate quality and quantity of labor

Practitioners ultimately give advice and make recommendations based on 3 principles

1. Research
2. Experience
3. Observations by veterinary peers.

Although this approach can be less than ideal, it is evident even from the literature that not all answers to questions regarding nursing calf pneumonia can be found. Nor can all questions be answered through research. For this reason, in investigation of outbreaks of clinical disease in beef herds, the use of a well-constructed list of risk factors is essential. The list of risk factors to be ruled out should become evident and recommendations for intervention and ultimately prevention can be implemented.

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