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Genetics, environment and bovine respiratory disease

Gary Snowder

National Center for Foreign Animal and Zoonotic Disease Defense, 200 Discovery Drive, College Station, TX 77843-2129, USA

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Abstract

The heritability estimates for resistance and/or susceptibility to bovine respiratory disease (BRD) are small, suggesting response to direct selection will be slow. The number of mammalian genetic markers associated with resistance to specific pathogens or improved immunity is increasing and will provide additional information for developing selection criteria for producing animals with an innate resistance to BRD. Environmental and management factors play significant roles in the prevalence of BRD and must be considered in a holistic approach to reducing BRD. Although no single solution for preventing BRD is likely to be discovered in the immediate future, the long-term outlook appears very promising.

Keywords: cattle, heritability, innate, selection, stress.

The phenotypic expression for resistance or susceptibility to a complex disease such as bovine respiratory disease (BRD) is influenced by both genetic and environmental factors. The genetic factors include the genetic constitutions of both the host and the pathogen(s). The host's innate ability to resist a pathogen is challenged by the pathogen's genetically influenced virulence. The environmental factors encompass climate, management, nutrition and production system. Environmental factors may suppress the expression of the host's genes for resistance, thus permitting the pathogen to propagate in the respiratory system. The interaction of genetic and environmental factors often determines whether or not an animal is infected and expresses the disease. No single solution, either genetic or environmental, should be expected to prevent BRD. The most likely solution to reducing the prevalence of BRD is a holistic approach addressing genetic, environmental, pathogenic and immunological factors.

Predisposing causes for BRD in pre-weaned and feedlot calves are generally concurrent, often synergistic, and include age, stress, immunological background, dehydration and nutritional stress (Callan and Garry, 2002; Duff and Galyean, 2007). In feedlot cattle, additional predisposing factors include weaning, shipping (method and distance), social restructuring, novel feedstuff and handling. Environmental risk factors to pre-weaned and feedlot calves include climate, ambient temperature, dust particles, exposure to noxious gases, stocking density, humidity and ventilation. Immune response in pre-weaned calves is influenced by passive immunoglobulin transfer and the innate immune system; whereas, in feedlot cattle the acquired and innate immune systems have a greater role to play in disease resistance. Epidemiological factors include microbial agent(s), mode of transmission, parasite density dependence, infectious period, latent and carrier period and virulence.

Episodes of BRD in pre-weaned calves are generally spatially and temporally periodic. In one study, the annual prevalence of BRD over a 20-year period (1983–2002) for pre-weaned calves ranged from 3 to 24% per year, with an average annual incidence of 10.5% (Fig. 1, Snowder *et al.*, 2005). In feedlot cattle, over a 15-year period (1987–2001) the annual prevalence ranged from 5 to 44% (Snowder *et al.*, 2006). The effect of climate on temporal BRD episodes may not be considered as the major explanation because the relationship between climate and BRD has not been clearly defined. A French study reported no clear trend between meteorological data and respiratory disorders in pre-weaned Charolais calves on 137 farms (Assie *et al.*, 2004). In Australian

E-mail: GDSnowder@ag.tamu.edu

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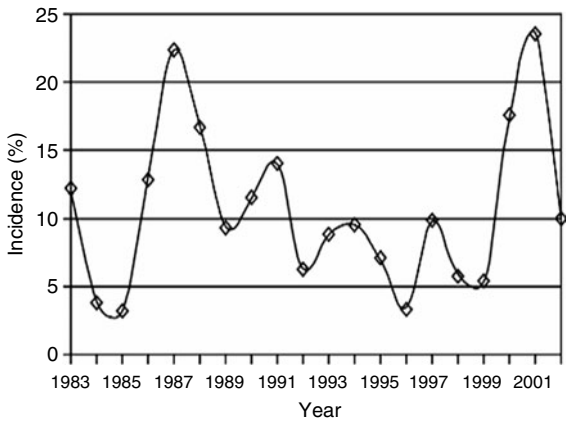


Fig. 1. Incidence rates by year of BRD in pre-weaned beef calves from 1983 to 2001 (Snowder *et al.,* 2005; reprinted with permission of the Journal of Animal Science).

research, the correlations between various climatic factors and incidence of BRD in feedlot cattle were generally low (Cusack *et al.*, 2007). Spatial effects such as pasture (Muggli-Cockett *et al.*, 1992), feedlot (Cusack *et al.*, 2007) or barn facility (Assie *et al.*, 2004) appear to be related to BRD episodes. Further research is needed to characterize spatial and temporal risk factors associated with BRD episodes.

The genetic factors influencing resistance to diseases, particularly BRD, have only recently been investigated. The heritability estimates for resistance to BRD in pre-weaned calves have been reported as low to moderate, ranging from 0.00 to 0.26 (Muggli-Cockett *et al.*, 1992; Snowder *et al.*, 2005). However, when the estimated heritability is adjusted to an underlying continuous scale, the estimate is large ($h^2 = 0.48$), inferring response to selection for BRD resistance could be large if the phenotype for BRD resistance was known (Snowder *et al.*, 2005). Breed differences are commonly reported. In a study comparing nine purebred and three composite breeds and a variety of F_1 and three-way crosses, including the progeny of 12 additional different sire breeds for susceptibility to BRD over a 20-year period, the lowest prevalence (9%) was observed in Hereford calves and highest prevalence (19%) in Braunvieh calves (Snowder *et al.*, 2005). Although conventional thought is that heterozygosity (hybrid vigor) has a positive effect on disease resistance, this relationship was not found to be significant for BRD resistance in pre-weaned calves (Snowder *et al.*, 2005).

In pre-weaned calves, the passively acquired maternal antibodies play a significant role in calf resistance to BRD. Maternal antibodies may provide protection for up to 3 or 4 months (Bryson, 1985). Therefore, the genetic potential of a dam to produce a high volume or concentration of maternal antibodies for BRD antigens may be a critical factor in reducing BRD in pre-weaned calves. However, large negative genetic correlations between dam and calf were reported (Snowder *et al.*, 2005), inferring that dams genetically superior for helping their calves resist BRD produce calves susceptible to BRD. One explanation may be that a dam's increased maternal genetic ability to produce and/or sustain production of immunoglobulins for BRD and to transmit these via lactation may delay the development of the calf's own immune system, thereby increasing the calf's susceptibility to BRD at a later age. A large negative genetic correlation between direct and maternal genetic effects might suggest that some degree of maternally imprinted major gene influencing BRD resistance is present.

In feedlot calves, heritability estimates were low and ranged from 0.04 to 0.08 (Snowder *et al.*, 2006). When the observed heritability estimate was transformed to an underlying continuous scale, the estimate increased to 0.18, again suggesting favorable response to selection if the phenotype for resistance to BRD was known. Thus, development of an inexpensive and humane method of challenging animals for BRD resistance would seem an important step in developing a selection program to reduce the prevalence of BRD.

The science of genomics may lead the way in defeating BRD in cattle. The physical map of the bovine genome provides cattle researchers with a tool to aid their search to improve health. Quantitative trait loci related to bovine health, including resistance to BRD, are just beginning to be discovered (Casas and Snowder, 2008). Additionally, biomarkers specific for bovine respiratory factors as determined by proteomics, metabonomics and immunology are helping to characterize the complex biological responses between host and pathogen (Aich *et al.*, 2009). Microarrays for bovine innate immunity are also being developed (Donaldson *et al.*, 2005), thus setting the stage for selecting healthier animals. As more genetic and biomarkers related to health are identified, the likelihood of being able to select for a genotype with resistance or improved immune response to pathogens greatly increases.

Prevalent microbial causes of BRD (Ellis, 2001) are of viral (infectious bovine rhinotracheitis, bovine viral diarrhea, bovine respiratory syncytial and parainfluenza type 3), bacterial (*Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni*) and mycoplasmal origins. Virulence of these pathogens can vary greatly across and within pathogens. Today's biotechnology has greatly enhanced our understanding of virulence factors within the pathogen's genome. Whole genomes including virulence genes have been identified in many pathogens associated with BRD, including *P. multocida* (May *et al.*, 2001). The cause of cytolysis of leukocytes observed with *M. haemolytica* infection in ruminants has been identified as CD18 on ruminant leukocytes serving as a receptor site for *M. haemolytica* leukotoxin (Zecchinon *et al.*, 2005; Fett *et al.*, 2008). Such knowledge of the pathogen may lead to more efficacious vaccines or prophylactic treatment, as well as selection for naturally resistant animals.

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As the level, frequency, and/or duration of stress factors increases the efficacy of the immune system generally decreases. However, this is not always true as the immune system actually responds favorably to some stresses (Salak-Johnson and McGlone, 2007). Duff and Galyean's (Duff and Galyean, 2007) review of management factors to reduce stress and prevalence of BRD concluded that preconditioning, vaccination and metaphylactic antimicrobial programs offer significant potential to decrease the incidence of BRD. However, nutritional manipulation to modify the incidence of BRD seems very limited.

Conclusion

In conclusion, genetics, environmental, stress and immunological factors have synergistic effects on BRD occurrence. As our comprehension of these numerous factors increases, the greater will be our likelihood of reducing BRD in livestock.

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