Bovine Respiratory Disease Prevention: Opportunities for Genetic Selection

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Summary

The Bovine Respiratory Disease (BRD) Complex Coordinated Agricultural Project (BRD CAP) is a 5-year USDA funded research project, the primary objective of which is to use genomics to identify cattle that are less susceptible to BRD. This paper describes the research progress made on this project to date including the identification of genetic markers associated with BRD susceptibility in Holstein cattle, scoring systems for the improved field diagnosis of BRD in pre-weaned dairy calves, survey results of California dairy calf rearing practices, and some practical findings and considerations of how all this information might be used in the future to select and manage calves to reduce the prevalence of BRD in the U.S. dairy industry.

Background

There is growing interest in the selective breeding of livestock for enhanced disease resistance. The dairy industry has a history of selection for a disease trait. Since 1994, selection programs have been developed to take advantage of genetic variability in mastitis resistance. Selection has been based on the indicator trait of somatic cell score (SCS), meaning that it provides a selection criterion which can be used to indicate which animals are less susceptible to mastitis. Currently, 7% of the emphasis in the 2014 Net Merit (NM$) index is assigned to lowering SCS. This is done despite the fact that the heritability of SCS is low (0.12) and mastitis resistance has an adverse correlation with production traits (Rupp and Boichard, 2003).

Bovine respiratory disease (BRD) is a disease of the lower respiratory tract of cattle that is multifactorial in origin and results in bronchopneumonia. It is commonly observed in dairy calves and has both acute and long term effects on the performance of those calves. Calves that were treated with antibiotics produced 493 kg less milk in the first lactation ($P > 0.01$) than calves with no record of being treated (Soberon et al., 2012).

Bovine respiratory disease is the largest single natural cause of death in US beef and dairy cattle, and BRD resistance represents an obvious target for selective breeding programs. However, unlike mastitis, there is no obvious indicator trait to use for selection against BRD. Given the multifactorial nature of BRD the genetic basis of BRD susceptibility is likely complex, and governed by the effects of multiple genes.

The heritability (h^2) of BRD susceptibility, defined as the proportion of observed variation that can be attributed to inherited genetic factors in contrast to environmental ones, tends to be low under field conditions. This is partly as a result of suboptimal diagnosis (i.e. not all sick animals are identified, healthy animals may be incorrectly diagnosed as ill, and some susceptible animals will appear resistant when in fact they have not been exposed to the disease agent (viruses and/or bacteria in the case of BRD)). These confounding factors add environmental noise to field data which decreases heritability. Field studies therefore likely underestimate the true importance of genetics in BRD incidence, and thus also undervalue the potential gains that could be made by breeding for disease resistance.

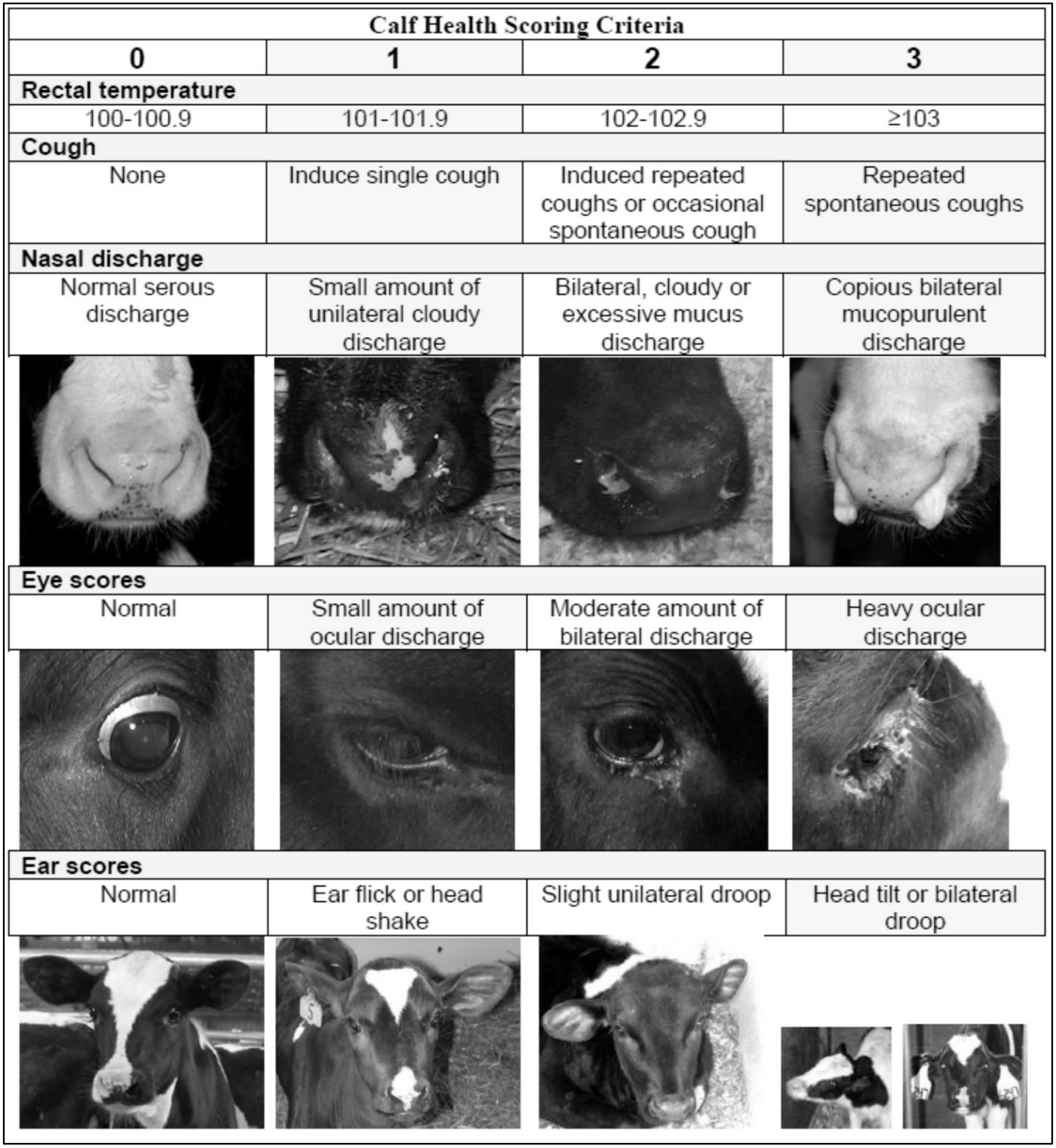
Newly-available genomic tools offer an opportunity to employ novel genetic approaches to select for more disease-resistant cattle. In 2011, the USDA AFRI funded a 5-year Coordinated Agricultural Project entitled "**Integrated Program for Reducing Bovine Respiratory Disease Complex (BRDC) in Beef and Dairy Cattle.**" The overarching research objective of this multi-institutional "BRD CAP" project is to use newly-available genomic tools to identify host genome regions associated with susceptibility to BRD.

As a part of this project, a large case:control study was undertaken to identify genetic markers associated with BRD susceptibility in pre-weaned Holstein calves. This paper describes the research progress made on this project to date, some of the practical findings and considerations, and how this information might be used in the future to select for cattle with reduced susceptibility to BRD.

Identification of genetic markers associated with BRD susceptibility

Pre-weaned Holstein calves between the ages of 27-60 days housed in hutches were observed in the early morning before feeding and were enrolled as a BRD case or control based on the McGuirk health scoring system (McGuirk, 2008). This standardized scoring system (**Figure 1**) relies on assigning a score of normal (0), slightly abnormal (1), abnormal (2), or severely abnormal (3) for each of 5 attributes: rectal temperature, cough, nasal discharge, eye discharge, and ear tilt. A calf with a cumulative score of ≥ 5 was assigned as a case, and a calf adjacent to that calf with a cumulative score of ≤ 3 was assigned as a control. A total of 1382 case calves, and 1396 control calves from a large dairy calf ranch in California (2,011 calves) and from dairies in New Mexico (767 calves) were enrolled in the trial. All calves were sampled for the identification of any bacterial and viral pathogens in their nasal or pharyngeal passages. The calves were also genotyped using a panel containing over 700,000 genetic markers known as single nucleotide polymorphisms (SNPs).

This information was then used to determine whether there were regions of the genome, as indicated by marker associations, associated with BRD susceptibility (Neibergs et al., 2014).



Calf Health Scoring Criteria

	0	1	2	3
Rectal temperature	100-100.9	101-101.9	102-102.9	≥103
Cough	None	Induce single cough	Induced repeated coughs or occasional spontaneous cough	Repeated spontaneous coughs
Nasal discharge	Normal serous discharge	Small amount of unilateral cloudy discharge	Bilateral, cloudy or excessive mucus discharge	Copious bilateral mucopurulent discharge
Eye scores	Normal	Small amount of ocular discharge	Moderate amount of bilateral discharge	Heavy ocular discharge
Ear scores	Normal	Ear flick or head shake	Slight unilateral droop	Head tilt or bilateral droop

Figure 1. The Calf Respiratory Scoring Criteria (McGuirk, 2008). Available for download at http://www.vetmed.wisc.edu/dms/fapm/fapmtools/8calf/calf_respiratory_scoring_chart.pdf

The observed pathogen profiles of the CA and NM animals differed for all pathogens with the exception of bovine herpes virus and bovine viral diarrhea virus, which were rarely detected in either population (**Table 1**). The genetic analysis of the study data showed moderate (~ 0.21) heritability estimates for BRD susceptibility in pre-weaned Holstein calves. This is higher than previous estimates of the heritability of BRD, likely due to the use of the standardized scoring system to objectively categorize cases and controls which minimized the probability that sick animals were not identified, and/or that healthy animals were incorrectly diagnosed as ill.

Table 1. *Pathogens identified from deep pharyngeal and mid-nasal swabs in pre-weaned Holstein calves from California and New Mexico*. Table reprinted from Neibergs et al. (2014).

Pathogen	***California** n = 2,014	***New Mexico** n = 748	**California & New Mexico** n = 2,763	**+Odds Ratio**	**Odds Ratio *P* value**
Arcanobacterium pyogenes	0.3 (0)	10.7 (4.3)	3.1 (1.2)	2.8	0.0003
Histophilus somni	1.7 (0.4)	3.2 (0.5)	2.1 (0.4)	4.9	<0.0001
Mannheimia haemolytica	23.5 (11.1)	4.5 (3.5)	18.4 (9)	2.3	<0.0001
Pasteurella multocida	36.3 (23.6)	61.1 (54.8)	43.0 (32)	1.6	<0.0001
Mycoplasma spp.	64.6 (57.1)	57.4 (48.7)	62.6 (54.8)	1.4	<0.0001
Bovine corona virus	9.6 (7.7)	50.0 (35.0)	19.9 (14.5)	1.5	0.0004
Bovine respiratory syncytial virus	20.8 (7.7)	4.9 (2.5)	16.3 (6.3)	2.9	<0.0001
Bovine viral diarrhea virus	0 (0)	1.3 (0)	0.4 (0)	NA	NA
Bovine herpes virus	0 (0)	0 (0)	0 (0)	NA	NA

*Percent of cases and controls (in parentheses) where individual pathogens were present in the pre-weaned Holstein calves. Animals classified as undetermined with respect to case-control status were not included in the summary statistics presented here.

+Odds ratio of being affected with BRDC when the pathogen was present when the animal was swabbed.

The analyses revealed approximately 116 genomic regions that were significantly associated with BRD in both the NM and CA populations, many of which were associated with biologically meaningful genes. Among them were genes that are known to mediate herpes virus entry into host cells, a gene associated with viral susceptibility, and a gene associated with inflammation. The fact that so many regions of interest were identified supports the idea that many genes are associated with susceptibility to this multifactorial disease. As with other "quantitative" traits associated with many genes, the best way to develop genomic-enhanced genetic merit estimates is to develop a genomic prediction for the trait based on the SNP genotype of the animal. Like other traits of economic importance to dairy production, the appropriate weighting to place on genetic merit estimates of BRD susceptibility will have to be calculated based on the relative economic value of this trait versus other traits of importance to dairy production in the NM$ index.

The importance of genetics as it relates to BRD susceptibility is illustrated by looking at the distribution of AI sires among the case:control calves that were enrolled in this study. Genotype information on AI sires was used to assign sires to the calves based on the 50K sire genotypes on file at the **Animal Improvement Programs Laboratory (AIPL).** A total of 1952 calves were sire-identified to a total of 707 AI sires. Approximately 370 of these sires had more than one calf. We examined the data on the 34 sires that had 10 or more calves represented in the data to determine whether sires generated case and control calves at an equal rate, or if there was a tendency for some sires to produce a disproportionately high number of either category. The data was tested for significance using a **chi-square** contingency table **analysis with Yates correction (Table 2).**

Table 2. *Number of cases, and controls sired by the 34 sires that sired ≥10 offspring in the BRD case:control study undertaken in pre-weaned Holstein calves* (unpublished BRD CAP data).

Sire	# offspring	# cases	# controls	% cases	% controls	$P < 0.05$
1	36	19	17	53%	47%	
2	30	12	18	40%	60%	
3	**25**	**18**	**7**	**72%**	**28 %**	**
4	19	11	8	58%	42%	
5	18	12	6	67%	33%	
6	18	12	6	67%	33%	
7	16	5	11	31 %	69%	
8	15	7	8	47%	53%	
9	15	9	6	60%	40%	
10	14	8	6	57%	43%	
11	14	10	4	71%	29%	
12	**14**	**3**	**11**	**21%**	**79%**	**
13	13	7	6	54%	46%	
14	13	8	5	62%	38%	
15	13	5	8	38%	62%	
16	13	9	4	69%	31%	
17	13	9	4	69%	31%	
18	13	4	9	31%	69%	
19	**13**	**12**	**1**	**92%**	**8%**	**
20	12	7	5	58%	42%	
21	12	5	7	42%	58%	
22	12	5	7	42 %	58%	
23	12	9	3	75%	25%	
24	11	6	5	55%	45%	
25	11	6	5	55%	45%	
26	11	5	6	45%	55%	
27	11	7	4	64%	36%	
28	11	4	7	36%	64%	
29	11	3	8	27%	73%	
30	**11**	**2**	**9**	**18%**	**82%**	**
31	10	6	4	60%	40%	
32	10	6	4	60%	40%	
33	10	7	3	70%	30%	
34	10	3	7	30%	70%	

It can be seen from Table 2 that some sires produce significantly higher than expected proportions of case (e.g. sire 3 and 19), and control (e.g. sire 12 and 30) calves. This simple analysis shows how the finding of a 0.21 heritability estimate for BRD susceptibility might play out on farm. If sire 12 and 30 have acceptable NM$, then their use could offer an approach to effect a sustained decrease in the incidence of BRD in dairy cattle. Future work includes further refining the genetic markers associated with BRD susceptibility, and working to incorporate genomic predictions for this trait into the national dairy cattle genetic evaluation scheme.

A Survey of California Dairy Calf Rearing Practices

A survey was designed to collect information about calf rearing practices on California dairies. Questions addressed calving and newborn calf management, colostrum management, pre-weaning calf management, and disease monitoring and prevention. Several methods were used to recruit responses from California dairy producers. Paper copies were mailed to 1,523 California Grade A milk producing dairies with the option to respond by mail or online. Responses were also recruited in-person at the World Ag Expo in Tulare, CA (2013) and by Cooperative Extension personnel. Responses were collected between February 2013 and January 2014. Both statewide and regional data were analyzed (Karle et al., 2014). Four geographic regions were identified: Northern California ("NC", Sacramento County and remaining northern counties), North Central Valley ("NV", San Joaquin to Madera Counties), South Central Valley ("SV", Fresno to Kern Counties) and Southern California ("SC", counties south of Kern).

In total, 234 respondents (15%) completed the survey. The average respondent herd size was 1420 milking cows (95% CI (1230, 1611)) which was larger than the 2013 California average herd size of 1164 cows/herd and may indicate a greater response rate from larger herds. The response rate was geographically consistent with the distribution of dairies in California with 40 responses from the NC region (16%), 96 from the NV region (18%), 78 from the SV region (14%), and 8 from the SC region (7%).

Of the respondents in NC, 70% left calves with their dams for greater than 1 hour after birth, compared to 44% in NV, 27% in SV, and 50% in SC. Of respondent dairies from NC and SC, the individual dam was the most common source of colostrum fed to heifer calves, 53% and 50%, respectively. In contrast, pooled colostrum was the most common source of colostrum fed to heifer calves on 58% and 63% of NV and SV respondent dairies, respectively. Statewide, 12% of respondents reported that colostrum was pasteurized and 32% measured IgG content in colostrum before feeding. In NC, 98% of respondent dairies raised pre-weaned calves on site. In contrast, approximately only half of the respondent dairies in the remaining regions raised pre-weaned calves onsite. Rather they contracted out heifer raising to specialized calf-raising operations. These calf ranches may have as many as 40,000 pre-weaned calves and a similar number of weaned calves in group pens. Statewide, waste or hospital milk was the most frequently reported source of milk fed to pre-weaned calves (72%).

A scoring system or an on-farm protocol was used to diagnose BRD on 21% of respondent dairies; however, based on our experience, we suspect these are primarily protocols based on simple observations rather than an objective scoring system. Cough (82%), depression (79%), ear droop (63%), nasal discharge (71%) and rapid respiration (77%) were the most common signs used to diagnose BRD on-farm. Listening to lung sounds using a stethoscope (22%), fever (25%), head tilt (34%), and eye discharge (27%) were less commonly used. The majority of respondents (83%) reported treating fewer than 5% of pre-weaned calves for BRD, although some were much higher and in the range of 26-50% (**Figure 2**). Intranasal respiratory vaccines were administered within 2 weeks of birth according to 50% of the respondents. A higher proportion of respondents reported rarely or never using killed respiratory vaccine compared to modified live vaccines (47% and 13%, respectively). This survey data will be combined with future research to develop and validate a BRD risk assessment tool to allow producers to identify calf management practices associated with BRD.

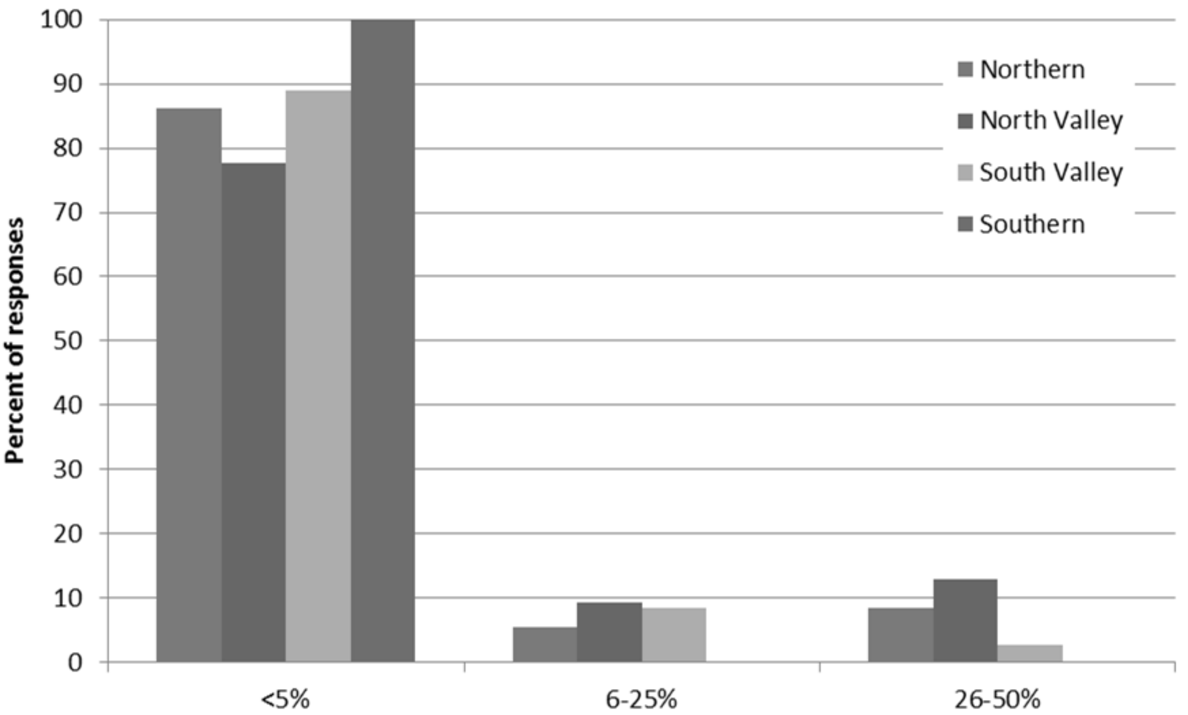
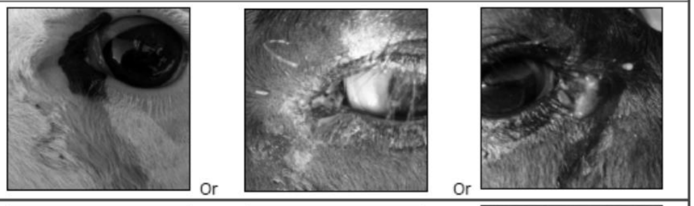
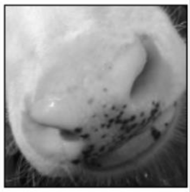
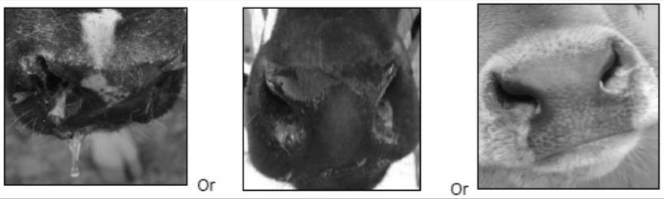


Figure 2. Percentage of pre-weaned calves that are typically being treated for pneumonia at any given time according to survey of California dairy producers (Karle et al., 2014).

A simplified BRD scoring system for pre-weaned dairy calves

Data from the large BRD case:control study was used to develop a simplified scoring system for pre-weaned calves. The rationale behind this development was the need to determine the BRD health status of a large number of calves on extensive calf-raising facilities in a relatively short amount of time, and the difficulty and time required to take temperature measurements on calves housed in California-style calf hutches. This simplified scoring used six clinical signs: eye discharge, spontaneous cough, breathing, fever (≥ 39.2°C/102.5°F), nasal discharge, and ear droop/head tilt each classified as either abnormal or normal. Each of the first 4 signs is assigned 2 points, nasal discharge is 4 points, and ear droop/head tilt is 5 points (**Figure 3**). A score of 5 or greater for this system called "BRD3" was determined to be the optimum cut-off to classify a case (Love et al., 2014), meaning that ear droop/head tilt is an automatic case. Users would need to obtain a temperature if the calf had a nasal discharge only, or only two of the other 2 point signs. This simplified scoring system had a 57% sensitivity for pneumonia and a specificity of 89.9% for calves without pneumonia (Aly et al., 2014), which were not significantly different from the values obtained for the WI scoring system shown in Figure 1. The comparable sensitivity and specificity, simple normal/abnormal categorization for each clinical sign, and the reduced calf handling may make this BRD3 scoring system advantageous for on-farm use, especially on large calf-raising facilities where hundreds if not thousands of calves may be evaluated daily.

Field diagnosis remains a challenge for the control and treatment of BRD, and it is hoped that this simplified standardized scoring system will be routinely used by dairy producers and calf raisers to diagnose cases of BRD on farm. It is available in both English and Spanish at the following URL: http://www.vmtrc.ucdavis.edu/laboratories/epilab/scoringsystem.pdf.

Clinical sign	**Score if normal**		**Score if abnormal** (any severity)[2]	
Eye discharge	**0**		**2**	
Nasal discharge	**0**		**4**	
Ear droop or Head tilt	**0**		**5**	
Cough	**0**	No cough	**2**	Spontaneous cough
Breathing	**0**	Normal	**2**	Rapid or difficult breathing
Temperature	**0**	< 102.5° F	**2**	≥ 102.5° F

Add scores for all clinical signs, if total score is ≥ 5, calf may be positive for bovine respiratory disease

<u>Figure 3</u>. The simplified BRD3 calf respiratory scoring system (Love et al., 2014).

The Future

Historically, breeding goals in dairy cattle focused on increased milk production. Selection for milk production has negative genetic correlations with many health and fitness traits, and there is a growing interest in including these traits in selection programs. It is interesting to view the evolution of the NM$ Index over time (**Table 3**). Two new fertility traits (heifer conception rate (HCR) and cow conception rate (CCR)) were included in the 2014 update to NM$ index. It is likely that more health traits will be included in future updates to the NM$ index.

Several studies show that the use of direct health observations is an effective way to incorporate heath traits into breeding programs. Such observations require a standardized system to record diagnoses to ensure phenotypes are comparable between farms. Consistent recording of health data is more difficult than for other traits due to subjectivity of diagnosis and reporting. Several studies have shown that for use in genetic evaluations, common health disorders recorded by farmers are of a similar quality as those documented by veterinarians (Egger-Danner et al., 2014). A recent study showed that genetic selection for health traits (including cystic ovaries, displaced abomasum, ketosis, lameness, mastitis, metritis, and retained placenta) using producer-recorded health data collected from on-farm computer systems is feasible in the United States (**Table 4**; Parker Gaddis et al., 2014). The authors go on to conclude that "The development of genomic selection methodologies, with accompanying substantial gains in reliability for low-heritability traits, may dramatically improve the feasibility of genetic improvement of dairy cow health."

Table 3. A history of the main changes in USDA genetic-economic indexes for dairy cattle and the percentage of relative emphasis on traits included in the indexes (VanRaden and Cole, 2014)

Traits included	USDA genetic-economic index (and year introduced)								
	PD$ (1971)	MFP$ (1976)	CY$ (1984)	NM$ (1994)	NM$ (2000)	NM$ (2003)	NM$ (2006)	NM$ (2010)	NM$ (2014)
Milk	52	27	−2	6	5	0	0	0	−1
Fat	48	46	45	25	21	22	23	19	22
Protein	…	27	53	43	36	33	23	16	20
Productive Life	…	…	…	20	14	11	17	22	19
Somatic Cell Score	…	…	…	−6	−9	−9	−9	−10	−7
Udder composite	…	…	…	…	7	7	6	7	8
Feet/legs composite	…	…	…	…	4	4	3	4	3
Body size composite	…	…	…	…	−4	−3	−4	−6	−5
Daughter Pregnancy Rate	…	…	…	…	…	7	9	11	7
Cow Conception Rate	…	…	…	…	…	…	…	…	2
Heifer Conception Rate	…	…	…	…	…	…	…	…	1
Calving Ability $ Index	…	…	…	…	…	…	6	5	5

<u>Table 4</u>. *Mean reliabilities of sire PTA computed with pedigree information and genomic information for health traits based on producer records of health events in U.S. dairy cattle. The right column shows how genomics can improve the overall gain* (Parker Gaddis et al., 2014).

Health Event	Pedigree information			Blended pedigree and genomic information			
	Overall mean	Unproven sires[1]	Proven sires[2]	Overall mean	Unproven sires	Proven sires	Overall gain[3]
Displaced abomasum	0.44	0.22	0.65	0.55	0.38	0.71	0.11
Ketosis	0.35	0.18	0.52	0.48	0.35	0.61	0.13
Lameness	0.24	0.15	0.32	0.39	0.31	0.47	0.15
Mastitis	0.39	0.26	0.52	0.51	0.40	0.612	0.12
Metritis	0.35	0.24	0.46	0.48	0.38	0.57	0.13
Retained Placenta	0.55	0.42	0.67	0.64	0.54	0.73	0.09

[1] Unproven sires considered sires with less than 10 daughters.
[2] Proven sires considered sires with at least 10 daughters.
[3] The increase in mean reliability calculated as the difference in overall mean reliability between the blended model and the traditional (pedigree data only) model.

Genomics has the potential to accelerate the rate of genetic improvement in low heritability, hard-to-measure traits such as disease status. However, phenotypes are still required to develop the genomic breeding values (GEBVs) for the trait of interest, and to keep the genetic marker effect estimates current. For BRD to become routinely included in dairy cattle genetic evaluations, standardized BRD health event data will need to be recorded on farm and fed into the national genetic evaluation system. To be successful, there needs to be a balance between the effort required to collect these data and subsequent benefits. Electronic systems that make such data capture easy and automated are likely key to the long-term success.

Summary

- Bovine respiratory disease (BRD) is a significant cause of morbidity, mortality, economic loss and is an animal welfare concern.
- Economic costs associated with BRD include treatment expense, mortality, premature culling, reduced growth, impaired fertility and reduced milk production in adulthood.
- Efforts are underway to develop large BRD case:control Holstein populations to enable the development of genomic breeding values (GEBVs) for BRD susceptibility.
- Preliminary data show BRD susceptibility has moderate heritability (0.13-0.21) suggesting there is an opportunity for improved animal health through selection.

- In the long-term, incorporation of BRD as a health trait into genetic evaluation programs will require a system to record standardized BRD diagnoses on farm to enable the development of a large data set of producer-recorded health data.

- Selection for animals with less susceptibility to BRD offers a promising long-term and permanent approach to decrease the incidence of this most common infectious disease and leading natural cause of death among cattle in the United States.

Acknowledgements

The authors acknowledge the Bovine Respiratory Disease Consortium Coordinated Agricultural Project (BRD CAP) team members and funding from the USDA Agriculture and Food Research Initiative (Competitive Grant no. 2011-68004-30367; J. E. Womack, PI) from the USDA National Institute of Food and Agriculture**.** The BRD3 scoring system was developed using case–control data that were collected as part of the BRD CAP. Development of the scoring system was funded by the University of California, Davis Division of Agriculture and Natural Resources (Grant no. 1753; S. S. Aly, PI). The authors thank the study dairies and calf ranch owners for their participation, and Mr. Paul Rossitto. More information about the BRD CAP can be found at http://www.brdcomplex.org/.

References

Aly, S. S., W. J. Love, D. R. Williams, T. W. Lehenbauer, A. L. Van Eenennaam, C. Drake, P. H. Kass, and T. B. Farver. 2014. Agreement between bovine respiratory disease scoring systems for pre-weaned dairy calves. Animal Health Research Reviews 15: 148-150.

Egger-Danner, C., J. B. Cole, J. E. Pryce, N. Gengler, B. Heringstad, A. Bradley, and K. F. Stock. 2014. Invited review: overview of new traits and phenotyping strategies in dairy cattle with a focus on functional traits. Animal : An International Journal of Animal Bioscience: 1-17.

Karle, B. M., W. J. Love , T. W. Lehenbauer, A. L. Van Eenennaam, L. Hulbert, and R. J. Anderson. 2014. A Survey of Calf Rearing Practices on California Dairies In: American Association of Bovine Practitioners (AABP), Albuquerque, NM

Love, W. J., T. W. Lehenbauer, P. H. Kass, A. L. Van Eenennaam, and S. S. Aly. 2014. Development of a novel clinical scoring system for on-farm diagnosis of bovine respiratory disease in pre-weaned dairy calves. PeerJ 2: e238.

McGuirk, S. M. 2008. Disease management of dairy calves and heifers. The Veterinary Clinics of North America. Food Animal Practice 24: 139-153.

Neibergs, H. M. et al. 2014. Susceptibility loci revealed for Bovine Respiratory Disease Complex in pre-weaned Holstein calves. BMC Genomics **15**:1164.

Parker Gaddis, K. L., J. B. Cole, J. S. Clay, and C. Maltecca. 2014. Genomic selection for producer-recorded health event data in US dairy cattle. Journal of Dairy Science 97: 3190-3199.

Rupp, R., and D. Boichard. 2003. Genetics of resistance to mastitis in dairy cattle. Veterinary research 34: 671-688.

Soberon, F., E. Raffrenato, R. W. Everett, and M. E. Van Amburgh. 2012. Preweaning milk replacer intake and effects on long-term productivity of dairy calves. Journal of Dairy Science 95: 783-793.

VanRaden, P. M., and J. B. Cole. 2014. Net merit as a measure of lifetime profit: 2014 revision. http://aipl.arsusda.gov/reference/nmcalc-2014.htm.

Notes: