

**BOVINE PULMONARY HYPERTENSION
AND CONGESTIVE HEART FAILURE
COLLABORATORS' WORKSHOP**

**September 18 – 19, 2018
Clay Center, Nebraska**



GREAT PLAINS VETERINARY EDUCATIONAL CENTER

School of Veterinary Medicine and Biomedical Sciences

UNIVERSITY OF
Nebraska
Lincoln®

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EXECUTIVE SUMMARY

Bovine congestive heart failure (BCHF) is increasingly recognized as an emerging condition of cattle in the Western Great Plains of the United States and Canada. BCHF is an untreatable, fatal condition involving pulmonary hypertension that culminates in right ventricular failure. Evidence suggests left-heart dysfunction may initiate BCHF in a significant number of cases at low and moderate altitudes. This feature is not present in cases of right-heart failure at high altitudes. BCHF outbreaks occur in operations feeding well-managed, high genetic merit cattle. For some producers, it is the single most costly health-related problem with losses exceeding \$250,000 annually in individual operations, even surpassing those from bovine respiratory disease. Consequently, reducing the impact of BCHF is a high priority for the cattle industry.

A workshop of collaborators was held September 18-19, 2018 at the UNL Great Plains Veterinary Educational Center to review current status of BCHF knowledge, identify gaps, and outline a plan for moving forward. Participants included researchers, veterinarians, cattle producers, and other beef industry stakeholders. Participants identified disease pathogenesis as a major gap in our BCHF knowledge including onset, progression, and risk factors associated with heart failure. Based on these knowledge gaps, the following critical needs were identified: diagnostic tests that allow rapid, early, and affordable identification of diseased individuals; knowledge of risk factors for disease (genetic, environmental, and management); and estimates of scope and economic impact of BCHF across North American cattle production. Meeting these critical needs will mitigate the impact of BCHF, enhance cattle health and welfare, and improve sustainability of beef production. Knowledge of BCHF pathogenesis also informs an important large animal model for human congestive heart failure associated with pulmonary hypertension and left heart dysfunction, and supports an integrative, multi-disciplinary One Health approach to optimize health for both humans and animals.

Bovine Pulmonary Hypertension and Congestive Heart Failure Collaborators' Workshop

September 18 – 19, 2018

University of Nebraska - Great Plains Veterinary Educational Center (GPVEC)

Objectives

1. Identify gaps in our knowledge of bovine pulmonary hypertension (PH) and associated congestive heart failure (CHF)
2. Prioritize research efforts for filling those gaps
3. Identify key individuals, institutions, and resources needed to accomplish the research
4. Develop a timetable for moving forward

Monday, September 17

6:30 p.m. Informal dinner at El Toro Mexican Restaurant, Hastings, Nebraska

Tuesday, September 18

8:00 a.m. Welcome and Opening Remarks
Dr. Brian Vander Ley
University of Nebraska - Great Plains Veterinary Educational Center (GPVEC)

8:15 a.m. Clinical perspective

8:15 – 8:45 Features of High Altitude Bovine PH/CHF
Dr. Frank Garry, Colorado State University

8:45 – 9:30 Emergence of Bovine PH/CHF in Western Plains Feedlot Cattle
Dr. Brian Vander Ley, University of Nebraska-Lincoln

9:30 – 10:15 Heartache in High Plains Feedyards – Not So High Mountain Disease
Dr. Greta Krafsur, University of Colorado – Denver

10:15 a.m. Break

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- 10:30 a.m. Producer perspective in a moderated panel discussion
The Impact of Feedlot PH/CHF
- 11:30 a.m. Lunch (provided by GPVEC)
- 12:30 p.m. The Importance of the Bovine PH/CHF Model in Studying Human PH/CHF
Dr. Dale Brown, University of Colorado-Denver
- 1:15 p.m. USMARC Beef Cattle Resources
Dr. Larry Kuehn, U.S. Meat Animal Research Center
- 1:30 p.m. In Search of a Genetic Cause and Diagnostic Markers for PH/CHF
Dr. Mike Heaton, U.S. Meat Animal Research Center
- 2:10 p.m. Developing a List of Key Knowledge Gaps Related to Bovine PH/CHF
Areas to Consider:
Genetic causes
Diagnostic tests
Uses of cattle as models for human PH/CHF
Disease mechanisms
Epidemiology:
Factors, characteristics and conditions associated with feedlot
PH/CHF
- 4:30 p.m. Adjourn
- 5:30 p.m. Dinner at the Fairfield Opera House, Fairfield, Nebraska

Wednesday, September 19

- 8:00 a.m. Finalize List of Knowledge Gaps
- 8:30 a.m. Establish a priority for Knowledge Gaps and provide rationale for
their order
- 11:00 a.m. Adjourn

Tour of U.S. MARC facilities available for interested parties

ATTENDANCE LIST & EMAIL ADDRESSES

MODERATOR

BRIAN VANDER LEY
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SPEAKERS

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BIOGRAPHICAL SKETCHES

MELODY BENJAMIN

Melody Benjamin serves as the staff liaison to the Animal Health and Nutrition Committee for Nebraska Cattlemen.

R. DALE BROWN

Dr. Brown is Senior Instructor in the Department of Pediatrics, University of Colorado-Denver. Dr. Brown's long term research focus is on signal transduction mechanisms in the cardiovascular system. His current research centers on the role of inflammatory processes in heart failure in response to pulmonary hypertension, using beef cattle as natural occurring animal models for human disease. Two paradigms under investigation are obesity-induced pulmonary hypertension and congestive heart failure in fattening beef cattle; and pulmonary hypertension-heart failure induced by chronic environmental hypoxia in cattle raised at high elevations. Dr. Brown received his Ph.D. from Rice University (Biochemistry, 1979), and completed postdoctoral training at University of California, San Diego (Molecular Pharmacology, 1979-1984). He has held faculty appointments at UCSD, University of Illinois-Chicago, and University of Colorado-Denver.

GARY DARNALL

Gary Darnall is the owner of Darnall Ranch, Inc. Darnall Ranch Inc. is a family owned ranch, feedlot and farm located in the Panhandle of Nebraska, 30 miles east of the Wyoming border and 30 miles southeast of Scottsbluff, Nebraska. This is a Commercial Angus cow herd utilizing composite angus/semimetal bulls. About 300-400 heifers are developed annually for

replacements. Bulls are selected utilizing EPD's and genomic data. The balance of the ranch offspring are fed out in the 22,500 head Certified Angus Beef commercial feedlot with records of conversion, rate of gain, grade & yield, and profitability analyzed each year. There is grassland, irrigated and dry land farm ground to support the cow/calf, yearling, and feedlot operations. The crop production is primarily utilized through the cattle operation. The short term goals for Darnall Ranch are to use genetics, heterosis and technology in the breeding herd to continually improve efficient performance and carcass quality for the best net value per cow.

GALEN FRENZEN

Galen Frenzen, his wife Gwen and son Eric have a 500 head seed stock (plus irrigated and dryland farming) operation near Fullerton, NE. He is past president of the Nebraska Cattlemen (2018) and is currently on the Board of Directors. He first became aware of this problem when visiting with feedlot operators and then his interest was enhanced when he heard Gretna Krafusur's presentation at the 2018 NCBA meeting in Denver. He feels there is a genetic link and that the process of addressing this problem needs to start with the seed stock producers.

The Frenzen's have had registered Polled Herefords since 1957 and registered Angus since 1979.

FRANKLYN GARRY

Franklyn Garry grew up on a diversified dairy farm in Upstate New York. He received his B.S. and DVM from Cornell University, and MS from The Ohio State University. He worked in a

dairy practice in upstate New York, and then advanced clinical training at the Maximilian University, Munich, Germany and at The Ohio State University. He is a specialist in the American College of Veterinary Internal Medicine. He is currently a Professor at Colorado State University, where he has been in the Department of Clinical Sciences since 1987. In addition to teaching and research, he has a part time appointment in Extension and has conducted numerous investigations of herd problems. Since 1996 he has been the coordinator of the Integrated Livestock Management program at CSU. This is a multidisciplinary graduate studies program that focuses research and training efforts at problems in cow/calf, feedlot, and dairy agriculture.

DALE GROTELUESCHEN

Dr. Grotelueschen's professional interests include beef cattle health systems management, preventive health strategy design, diagnostic investigations, also including factors influencing morbidity and mortality, control of bovine viral diarrhea virus, neonatal calf diarrhea, and bovine respiratory disease. He has served as Director of GPVEC since 2013 following service as a managing veterinarian, Beef Cattle Veterinary Operations, Pfizer Animal Health 12 years, with the University of Nebraska 16 years as professor Veterinary Extension and Diagnostics and as Director of the Panhandle Veterinary Diagnostic Laboratory, Scottsbluff, Nebraska, and in private veterinary practice for 11 years, mostly in southwest Nebraska.

He is active in organized veterinary medicine and the beef industry. He received his DVM from the University of Missouri and MS, Clinical Sciences from Colorado State University. He and his wife, Elizabeth, are parents of 2 grown daughters and reside in Harvard, Nebraska.

DEB HAMERNIK

Deb Hamernik is Associate Vice Chancellor for Research; Associate Director, Nebraska Agricultural Experiment Station; and Professor, Department of Animal Science at the University of Nebraska-Lincoln (UNL). She administers sponsored funding and helps faculty build interdisciplinary research teams. She was National Program Leader, Animal Physiology at the USDA Cooperative State Research, Education and Extension Service and Scientific Review Administrator at the NIH.

Deb is a native Nebraskan and earned a B.S. from UNL in animal science; M.S. from Washington State University in animal science; and Ph.D. from Colorado State University in animal physiology. She received an NIH National Research Service Award to conduct postdoctoral research in the Department of Pharmacology at Case Western Reserve University.

MIKE HEATON

Mike Heaton received a BS in Biological Sciences and a PhD in Chemistry from the University of Nebraska-Lincoln and did postdoctoral research at Northwestern University and The Rockefeller University. Prior to joining the USDA in 1996, his research focused on the bacterial cell wall as a target for antibiotics and the spread of antibiotic resistance genes among hospital isolates.

At the USDA, his research is centered on genomics of the host-pathogen interaction, and includes DNA-based traceback of diseased animals. In December of 2003, he and his colleagues traced the first U.S. mad cow case to its Canadian origin with parentage markers. In 2012 he reported the discovery of a lentivirus susceptibility gene in sheep (TMEM154). In

livestock, this was the first example of a genome-wide association study identifying a major gene that affects susceptibility to an infectious disease (ovine progressive pneumonia, OPP). His current research is directed towards finding bovine gene variants that are risk factors for respiratory infections.

CLAYTON KELLING

Clayton Kelling is a native of western North Dakota USA, where he grew up on a cow-calf operation near Killdeer.

Kelling received a DVM from Iowa State University College of Veterinary Medicine. He earned a PhD and MS in animal science/veterinary science and a BS in agriculture from North Dakota State University.

He joined the faculty in the University of Nebraska–Lincoln (UNL) Department of Veterinary Science in 1976, and established and directed the veterinary diagnostic virology laboratory in the Nebraska Veterinary Diagnostic Center and conducted pseudorabies research and bovine respiratory disease research. While attending veterinary school, he worked at the Veterinary Medical Research Institute in the College of Veterinary Medicine at Iowa State University (ISU) and conducted research on bovine viral diarrhoea virus. The research was a joint project funded by ISU and UNL.

Currently, Dr. Kelling is a professor and director of the UNL School of Veterinary Medicine and Biomedical Sciences.

GRETA KRAFSUR

Greta M. Krafsur grew up on a 4th generation diversified family farm in Eastern South Dakota that continues to be owned and operated by her family. Greta took the circuitous route to

veterinary school, completing graduate studies in Nonwovens Science and Engineering and raising her 3 sons, Joseph (20) and twins (Benjamin and Joshua-18) before commencing her veterinary studies at Colorado State University where she graduated with honors and then went on to complete residency training in anatomic pathology.

A diplomate of the American College of Veterinary Pathologists, Greta chose to specialize in production animal diseases, specifically beef cattle and in 2015 was recognized by the National Cattleman's Beef Association with the W.D. Farr Scholarship. Greta's enthusiasm for beef cattle has taken her across the pond twice, first seeing farm animal practice in rural Scotland in 2013 and in 2017 as a delegate to the World Angus Forum in Scotland.

LARRY KUEHN

Dr. Kuehn has been a Research Geneticist at the U.S. Meat Animal Research Center since 2006. He is a co-leader of the USMARC Germplasm Evaluation (GPE) program including sampling and mating industry representative sires from 18 beef breed associations and subsequent phenotyping of offspring for economically relevant traits. He leads efforts in genetics of bovine respiratory disease susceptibility and finishing steer and growing heifer feed efficiency using subsets of the GPE population. The GPE population is also the primary beef resource for genomic discovery at USMARC and has been extensively genotyped with high-density marker arrays.

In addition, Dr. Kuehn, with his collaborators, has coordinated DNA collection from several industry partners to facilitate further genetic research in novel traits such as bovine

respiratory disease, reproductive fitness, and liver abscesses. Dr. Kuehn serves as acting research leader for the Genetics, Breeding, and Animal Health Research Unit.

SCOTT MACGREGOR

Scott MacGregor is a feed yard veterinarian and has worked with the Dinklage group for 15 years. He is currently with Feedlot Health-USA/MacGregor Consulting and is semi-retired.

DAN MOSER

Dan Moser is President of Angus Genetics, Inc., and Director of Performance Programs for the American Angus Association, headquartered in St. Joseph, Missouri. He is also a Collaborator with Colorado State University on genetic evaluation of pulmonary arterial pressure in Angus cattle, and Director of the Beef Improvement Federation. He was previously Associate Professor of Beef Cattle Genetics, Department of Animal Sciences and Industry, at Kansas State University.

ROD MOXLEY

Dr. Rod Moxley received his DVM in 1978 and his Ph.D. (Pathology) in 1983 from the University of Missouri – Columbia. His current positions include: Charles Bessey Professor, School of Veterinary Medicine & Biomedical Sciences, University of Nebraska – Lincoln; Director of the Shiga toxin-producing Escherichia coli (STEC) USDA-NIFA Coordinated Agricultural Project; and Co-Director of National Institute for Antimicrobial Resistance Research and Education (sponsored by APLU and AAVMC)

BILL RISHEL

Bill Rishel is past owner/operator of Rishel Angus, seedstock operation, in North Platte,

Nebraska, which was one of the very first breeding programs in the beef cattle industry to prioritize structured sire evaluation for carcass merit. Industry service: Board of Directors of NCBA, BOD of American Angus Association, BOD of Certified and Beef Program (chair), Cattlemen's Beef Board, BOD Nebraska Cattlemen, President of Nebraska Cattlemen 2010, Long Range Planning Task Force NCBA, Chairmen Product Enhancement NCBA, Beef Quality Audits NCBA. Bill is currently serving on the Nomination Committee- Nebraska Cattlemen, Carcass Grading subcommittee NCBA, Resource Council NCBA, Beef Focus Group US MARC, and is still engaged in Purebred Angus business as advisor to T/D Angus at Rishel Ranch, North Platte, Nebraska.

JUSTIN SEXTEN

Justin Sexten is the Director of Supply Development for Certified Angus Beef, LLC, in Wooster, OH. In this role he leads production research and producer education initiatives with emphasis on high-quality beef production. He was previously an Assistant Extension Professor of Beef Cattle Nutrition, Division of Animal Sciences, at the University of Missouri. Justin earned his Ph.D. in Ruminant Nutrition from the University of Illinois with emphasis in replacement heifer development.

KURT STENMARK

Dr. Stenmark is Professor of Pediatrics, Medicine, Anesthesiology, Head of the Division of Pediatric Critical Care Medicine and Director, Cardiovascular Pulmonary Research Laboratory at the University of Colorado Denver (UCD) and The Children's Hospital Colorado in Aurora, Colorado. He joined the Pediatric faculty at UCD in 1984 as an Assistant Professor, was made Associate Professor with Tenure in 1989, and full Professor with Tenure in 1994. He has

been the Division Head of Pediatric Critical Care Medicine since 1987.

Co-author of over 330 publications, Dr. Stenmark is currently Principal Investigator on a number of NIH grants (including a PPG, R01, and a T-32 Training Grant) in the areas of immature pulmonary circulation, hypoxic vascular modeling, and pediatric pulmonary disease. Additionally, he provides research support on a number of other NIH grants. The NIH has continuously funded him since 1984. He has received numerous international honors and awards, sits on several national and international committees as well as major grant review committees in his field (permanent member of RIBT and NHLBI).

He currently serves as an Associate Editor for American Journal of Physiology, Lung, Cellular, and Molecular Physiology and is on the Editorial Board for several noted journals. Dr. Stenmark has been a visiting professor or invited speaker throughout Europe and North America. He is the honored recipient of the 2015 Robert F. Grover Prize from the American Thoracic Society for excellence and long-standing contribution to pulmonary vascular diseases.

BRIAN VANDER LEY

Brian Vander Ley grew up on a small, diversified farm in South Dakota. He completed his undergraduate studies at Dordt College in Sioux Center, Iowa and went on to attend Iowa State University to earn both his DVM and PhD degrees. While completing his post-DVM education, Dr. Vander Ley also completed a clinical internship with the Iowa State University Food Animal Medicine and Surgery Service and served as an emergency food animal clinician. Dr. Vander Ley was previously a faculty member at the University of Missouri

from 2012 until 2016 where he served as an ambulatory food animal clinician and conducted research aimed at managing bovine respiratory disease.

In 2016, Dr. Vander Ley joined the faculty at the University of Nebraska-Lincoln Great Plains Veterinary Educational Center. His current research focuses on congestive heart failure in feedlot cattle and population level disease surveillance. He is also actively engaged in teaching epidemiology to graduate students and veterinary extension efforts across Nebraska.

TOM WILLIAMS

Tom Williams is part owner and general manager of Chappell Feedlot at Chappell, Nebraska. He purchased the feedlot in 1992 from the Merlyn Carlson family, for whom he was ranch foreman for 10 years prior to purchasing the lot. Chappell Feedlot ownership is primarily a custom yard, focusing on retained ownership cattle.



"Working for Nebraska beef producers - pasture to plate."

October 23, 2018

Brian Vander Ley, DMV, PhD, DACVPM
Veterinary Epidemiologist
Great Plains Veterinary Educational Center
P.O. Box 148
Clay Center, NE 68933

Dear Dr. Vander Ley,

I would like to express Nebraska Cattlemen's strong support for the need to investigate and solve bovine congestive heart failure (BCHF). BCHF is increasingly recognized as an emerging condition of cattle in the Western Great Plains of the United States and Canada.

Our organization's mission is "Working for Nebraska beef producers – pasture to plate." We have a vested interest in solving BCHF and keeping our members informed. It has a significant impact on the economic viability of the operations of our members. We plan to conduct a survey to determine how large the impact is, both economically and with employee morale.

I believe research is important, feasible, and consistent with the goals of our organization. It will provide valuable information and guidance to our livestock producers.

Sincerely,

A handwritten signature in black ink that reads "Pete McClymont". The signature is written in a cursive, flowing style.

Pete McClymont
Executive Vice President & Treasurer

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To Whom It May Concern:

Re: Letter of support for further Bovine Congestive Heart Failure (BCHF) research

As a custom feedlot owner and manager, I am elated that this elite group of veterinarians and scientists have taken a high degree of interest in Bovine Congestive Heart Failure (BCHF). The initial study conducted by this team involving 102 cases at our feedyard and three other yards has already led to a higher level of understanding this problem. This study provided a baseline of multiple factors from which to build on with further research to identify genetic factors, improved testing methods to identify individual risk animals, and other management factors to lower the incidence of this disease.

At CFL, we identified this problem 20 years ago when we found the acute form of BCHF in the form of aneurysms in the pulmonary artery, aorta, or even the heart itself. It occurs mostly in calf feds, so over time we realized we should grow those cattle longer, not push these younger cattle as quickly. That has almost eliminated the acute form, but now we mostly see the chronic form as a result. So at the end of the day the death losses are static and increasing some years. From an economic and animal welfare standpoint, the acute form is actually the better endpoint, with quick and painless death. Most of our feeding clientele are ranchers, and dead slips are never welcome. At least as we gain more knowledge of the problem we can work with them to improve the genetics, etc. We have lost customers due entirely to BCHF losses. Not to mention it is a helpless feeling for pen riders not being able to do anything for these cattle, and ultimately having to euthanize them.

It is of great importance that this team continues to build on this valuable initial study with more research, the economic and emotional ramifications possible are huge. The similarities to the same human condition particularly stimulate the need for more joint research.

Tom Williams
Chappell Feedlot



Bus. (308) 783-2048
Res. (308) 783-1456

3071 Road 67
Harrisburg, Nebraska 69345

Date: 10/25/18

To: Whom it May Concern

Re: Letter of Support for solving BCHF (Bovine Congestive Heart Failure)

We at Darnall Ranch Inc. and Darnall Feedlot would like to submit a letter of support for solving BCHF. This problem impacts us and the industry as a whole in several ways. Speaking from our point of view – the areas of impact are as follows :

- a. Economic: In the past 5 years we have seen 518 head of BCHF in our feedlot including deads and realizers. This calculates to a financial loss of \$943,553.00.
- b. Labor: BCHF accounts for .52% of the deads and realizers in the feedlot. This is the highest death loss we have other than respiratory out of the 22 categories we have to diagnosis a death. Every BCHF dies and there is not treatment. Our pen riders check every pen of cattle daily. There is time and labor to correctly identify these animals so that extra time and medicine costs are not incurred. Our own health crew, in the early stages of diagnosis, often treat animals as respiratory with time and medication, sometimes racking up a large medicine bill, only to find they are actually a brisket.
- c. Employee morale: We are fortunate in that most pen riders identify with being able to pull, treat, and restore sick animals back to health. It is a sense of pride they share doing this. It is very depressing to find and identify animals that you know have no hope – they will die and die soon.
- d. Customer satisfaction: We pride ourselves here at Darnall Feedlot at accurate identification of disease, appropriate treatment and accurate identification of causes of death, through a post mortem exam. We give all these results to the customer. While we pride ourselves in doing a good job at this – other yards may not go to this much work or effort. They

come across as not having as many briskets (if they are not identified correctly). We have had customers say that they will go to this yard or that yard as they don't have as much incidence of BCHF as we do. So us doing a good job seems to shoot us in the foot.....

Having a tool to identify these animals before we spend and lot of time, money, and medicine into these animals would benefit all of the above listed problems.

In summary, we support efforts to find a way to solve BCHF or at the very least find an easily used and affordable method of identification of BCHF animals early in their life to effect a different outcome for the animal.

Sincerely,

A handwritten signature in cursive script that reads "Geoff Darnall". The signature is written in black ink and is positioned below the word "Sincerely,".