## Calving Distribution and Herd Health

## Season 1, Episode 8

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**Olivia Amundson:** Welcome back to another episode of cattle HQ brought to you by South Dakota State University extension, I am Olivia Amundson based out of the Sioux Falls regional office. Here, with my colleague Kiernan Brant located out of the Watertown regional office today we'll be talking to Dr. Brian VanDerLey on congestive heart failure in feed lot cattle. Brian, would you mind, giving us a brief introduction.

**Dr. Brian VanDerLey:** Yeah so my name is Brian VanDerLey I work out at the USDA Meat Animal Research Center but I’m actually a UNL University of Nebraska Lincoln employee. And to keep the centers apart, I work at the Great Plains Veterinarian Educational Center that's on that campus. So out there I do some quite a bit of research, but I also do some veterinary student teaching and graduate student education, and I also work for the University of Nebraska Extension.

**Olivia Amundson:** You got a lot of different hats sounds like um yeah, Kiernan and I actually we had a conversation, a few days prior and got to talking about how both him and I have had some experience down at the Meat Animal Research Center. I spent a little bit of time down there doing an internship with Jeremy Miles and then did my graduate work with Dr. Cushman and Dr. Harvey Freetly, but then I also worked at the Great Plains Vet Education Center having worked with Dr. Dale Grotolusheun and Kathy Whitman, so I have had a little bit of experience down there and as well as Kiernan.

**Kiernan Brandt:** Yeah I think we got to talking about just some of the good old days at the Meat Animal Research Center and I just think it's super super funny how like the further we get into this realm in this this industry, the smaller the world really gets. Like Olivia and I have quite a bit of history in that regard I ended up citing her a bunch in like my graduate research, just have her become a co-worker, on the other side of the country, a few months, a few months later and yeah find out with that we both spent time at the Meat Animal Research Center which at the time I hadn't no idea what really that beast was and how widespread the impacts that come out of that place where I was just a kid that didn't come from an ag background that was trying to get some more experienced during the summers while I was going to undergrad in Laramie and it was during one of the last hiring freezes actually, and so I ended up having to be a UNL summer employee rather than do any formal work through USDA or anything like that, but, I think, even at that point, I had an appreciation for some of the stuff that was going on, but really did not did not have quite the full picture of how much stuff is going on at MARC and how how cutting edge, a lot of that research is going on and I thought it'd be cool Brian if you just wanted to talk for a second about what's going on down there, right now, what are you guys working on it at the Great Plains Vet lab and what's MARC interested in right now and what are all the bigwigs down there working on.

**Dr. Brian VanDerLey:** Well, let me start with MARC I can't give you a very detailed overview there's a lot of research that happens in US MARC, I think it holds the distinction of being the largest live animal based research institution in the world there's a lot of so there's about 8000 mother cows that live at US MARC there's about 1000 sows and there's about 2000 to 3000 sheep out there at any one time so they're doing research on all those species there's a tremendous amount of emphasis put on genetic work genetic research out of the US Meat Animal Research Center they're highly capable and very well equipped to do genetic work. State of the art sequencing and many other facilities that allow them to do that stuff. They also do a lot of nutrition and reproductive physiology and meats, including food safety research out of US MARC. So a great variety of things going on the group that I work most closely with and what we're going to talk about today a little bit is the genetics of animal health research unit does work looking at mostly cattle, but also some sheep diseases and, and we are interested, particularly in in some infectious diseases. A lot of things going on with coronavirus and bovine growth diarrhea virus there's some immunology work that's ongoing, as well as some work with mannheimia and a couple of the other bacteria that are implicated for respiratory disease, but my principal collaborator over at the US Meat Animal Research Center, Dr. Mike Heaton and he and I, together, have really spearheaded the project to look at this this congestive heart failure problem and feed cattle.

**Kiernan Brandt:** No, I was when I was looking through your background and one of the many hats you wear is veterinary epidemiologist and I thought that was interesting that I guess I just didn't put those things together right off the bat that an epidemiologist would be climbing into the genetic cesspool, if you will, that that can often turn into when you start chasing these rabbit holes and things like that. Can you just give us some backstory on how you got involved in looking at congestive heart failure, and in some of these feedlot animals.

**Dr. Brian VanDerLey:** The first thing I should probably say is that epidemiology is basically the discipline that people who can't make up their minds get into. Epidemiology has the, yeah I tell my students all the time epidemiology is the science of associations, so we don't. We don't have to pick a realm too tightly and stick to it, we can move around a lot, and the reason I'm involved in this particular work is because we're looking at a number of associations and the most interesting and the most research that we have right now in terms of results is in the association with heart failure and genetics. But we are also very interested in the associations between management and environment in this particular disease, because we're pretty sure there's some of that going on to we just don't have a lot of evidence for yet, we're kind of in that anecdotal or early descriptive evidence stage when we started describing some of those management environmental factors but yeah try to you know, try to put an epidemiologist in a in a corner, with regard to like, we're given a lot of latitude to look for things that are associated with each other so it's a, it's a good discipline for me to be part of.

**Olivia Amundson:** Yeah and so you talk a lot about congestive heart failure in cattle this traditionally or has historically been associated with a higher altitude sort of situation. But tell us a little bit about what you're learning about congestive heart failure because you mentioned genetics, a lot.

**Dr. Brian VanDerLey:** yeah so, one of the things that Dr Mike Heaten, at US MARC when I first got involved in this research pointed out to me, as he said, there are certain diseases that give you really strong indicators that they’re genetic. One of the indicators that we have observed very frequently with the disease that we're interested in here, which is heart failure and feedlot cattle is that will have the same groups of cattle from the same source, year after year have problems right next to groups of cattle from other sources that don't. So the, the, in other words, the problem is very much clustered within sources, we tend to see these clusters of cases that come from you know pretty unique and consistent genetic pools. I'm not going to say genetic lines, because we don't really worry about that too much, but the same sources, the cattle from the same operations will consistently produce high numbers of these cases and we tend to see them year after year, produce a bunch of cases and in the same environment, the same feed lot with roughly the same nutrition things like that will be other groups cattle that have almost no problems. Which is a pretty strong indicator that there's some sort of unique factor about the place those animals are coming from that makes them more susceptible or, more likely to get this disease and genetics, is one of the one of the strongest factors when you start seeing a lot of diversity of sources, you know we were seeing sources that had a lot of cases that were coming from all over kind of I would call it the high plains region in some of these feedlots that we were we were getting reports of a lot of heart failure cases in, and that even more strongly implicates genetics as a as a factor. The other thing that's pretty strong implication is, in this case, we tend to see it, and we do have the evidence to support this, it does seem to be in British cattle, especially Angus when almost all the cattle. So as an epidemiologist it's really difficult, it's a little complicated say what I'm about ready to say but it's not fair to say that all the heart failure cases show up with black cattle so it's an Angus problem without actually showing that it's an Angus problem genetically because almost all the cattle that get fed in high plains, or a huge percentage of them are actually Angus cattle. So we can mistakenly draw some lines between breeds with, especially the Angus breed because it's so common, but in this case we've actually done the work to show that it really is, it's most significantly associated with the Angus breed.

**Kiernan Brandt:** I think a lot of guys in this part of the world obviously, have those type of genetics already prevalently utilized in their operations, but I did think that was super interesting that you guys were seeing it almost well not exclusively by any means, but definitely predominantly in those black hided cattle and I guess just before we get any further down talking into the specifics of what the impacts of this disease can look like and the effects that it can have and how we can kind of manage it a little bit better. Can you give us a little bit more insight into what exactly is going on in the heart when these problems manifest because there's some different things that can cause the heart to fail right, but this is pretty specific?

**Dr. Brain VanDerLey:** Yeah, this is actually kind of it's almost a diagnosis of exclusion at this point because we see a lot of different ways that heart failure can occur so there's three big buckets you can put heart failures into. One bucket is the medical term is diastolic dysfunction so that's basically the inability of the heart to adequately fill when it's relaxed, because the heart doesn't fill through vacuum it fills through the inherent pressure that's in the blood vessels so that pressure causes blood to flow into the heart when it relaxes so it's a very passive filling and when anything puts pressure on the outside of the heart it's really difficult for that heart to completely fill in and eject a full, like the largest volume of blood per stroke possible. So as the heart loses its ability to fill appropriately it actually starts to decrease in its cardiac like the cardiac output goes down. And that will actually cause a backup of blood in the body that will manifest this heart failure and we'll see that in cases like hardware disease, where an animal gets an infection that produces a lot of fluid around the heart. That fluid will actually start creating some pressure around the heart that prevents it from filling and we'll see the very same signs that we see with high elevation heart failure or any other kind of heart failure show up and it's because of the hardware. We can also see problems with the power stroke, the systolic function of the heart when it doesn't adequately pump when that muscle is compromised will see that a lot of times with things like toxins, the most common that we see as ionophores like rumensin or monensin and lasalocid and what those things do is they basically damage the muscle, so that it can't generate as much force when it goes to contract blood or expel blood from the heart. So, the third kind is what we see it altitude, which is basically a resistance to outflow so when an animal especially cattle when they get up in high ovations, we usually think about 5000 some people use above 7000 feet of elevation the shortage of oxygen actually causes little arteries in the lungs to constrict and that's in normal circumstances and that's usually really protective for the animal, because if it's a little bit of the lung gets disease. They want to actually shut down blood flow to the diseased area because it's not getting any oxygen anyway. So they maintain a rich supply of oxygen by actually shutting down blood flow to places where it can't get any. What happens at altitude, is it basically does that throughout the whole one field, and when that happens, it puts tremendous back pressure on the heart and it over time that actually makes the heart fail. So those are the three basic kinds of heart failure we see all kinds of causes so lymphoma is somewhat rare in cattle, but it happens with some frequency and that will cause heart failure if it forms a mass around the heart. We’ll see sometimes chronic pneumonias will get a version very similar to that see that high elevation but, in our case, what we see is, well, first of all it's none of those things like we ruled all those things out so it's none of those. And what's unique about the type of heart failure we see, is it looks a lot like what we see at a high elevation but instead of just affecting the right ventricle, which is the case with high elevation disease, we see it, affecting both right and left ventricle. So it's a different it's a different presentation of disease and we also don't see it just at high elevation we see this disease show up in cattle at 4000 feet, we've got cases at 1600 feet. We've even got a few cases are quite a bit lower than that so it's a little bit different it's really important when we did our research to do necropsies, to make sure it's not one of the other things.

**Kiernan Brandt:** Yeah I think that's a that's a really good point that's kind of why I wanted to get you into that and give us a little bit more idea of what these guys could be looking for on affected animals that they might not be able to identify because, I just, some people I talked to in this part of the world have had experiences with it and kind of recognize what it looks like. Others have not seen it and I think that could potentially become a problem if they start to have an outbreak or something like that and have no experience dealing with it, I think that could put some put some guys in a corner. So in the early stages, I mean, obviously I did my undergrad in Laramie so I was used to interacting a little bit with Tim Holt coming up and doing some PAP scoring on those yaks and yak crosses to they were doing a lot of that research at the at the time. Is that where you guys started with this trying to look at maybe some PAP measurements some arterial pressure and, like the heritability aspect there of trying to get it out of these cattle.

**Dr. Brian VanDerLey:** So, I think the best answer that question that predates my time at GPVEC a little bit, but the best answer that question is probably that our approach was different and the way our approach was different is that, so one of the things that Dr. Heaton has given me a little bit of education on is that there's a couple different kind of geneticists out there, I didn't know that when I started working at US MARC, but now I do. So quantitative geneticists are the folks that are very much interested in in getting a lot of SNPS and associate, they're also scientists of association. They associate different regions of the genome with outcomes and those outcomes, though, you know we're all very familiar with that that it can be weight, you know things like yearling, weaning weight, ugh marbling all those types of parameters and PAP, is one that they've tried to do that with. Dr. Heaton is a, so he I think he refers to himself as a molecular geneticist and the principal differences that he's very much interested in finding mutations that have biological outcomes. So the process of figuring out where those mutations is, is somewhat different, but it starts from the perspective that we're not going to worry about pedigrees and heritability and a lot of those kind of typical genomic approaches to genetics, but instead we're going to look for differences between animals that are very closely related, both in genetics and management and environment. And we're going to look at the genetic code of those animals and find differences and if we match them closely enough, we assume that those are likely differences contributing to the difference in outcome in other in this case would be whether or not they got heart failure not. And in fact that that approach for diseases actually works quite well because we assume that most diseases are a loss of function of some kind in the genetic code. When we are looking for the genetics of disease, rather than doing broad associations looking for biological functions can be a pretty powerful approach both can have value, but in this case it's quite a bit, you know it's quite a bit easier when you think about, at least for me I'll put this in my in terms of my understanding, but it's quite a bit easier for me to think about breeding away from a mutation than it is to think about breeding away, or, breeding toward an EPD target or something like that it's a little bit more amorphous. And so, this you know good examples of that would be you know some of the common mutations that we see in livestock we've, for instance, horns is a in a lot will pull this sort of a loss of function for the growth of horns that might not be how to this is think about it, but that's kind of how I'm thinking about it here. But it's pretty easy to breed away, you know it's a binomial outcome right or a yes or no, we either have horns on an animal or we don't. And it's relatively easy to breed away from horns, if we want to as opposed to trying to breed shorter and shorter horns until they disappear right. So a little bit different that's a little bit about how I think about quantitative genetics. So in this case, what we're trying to do is figure out how to turn the switch switches on and off. Not have less and less now to some extent we're still going to see less and less of it occur like we're not going to get rid of all of it because we're starting to find out that again there's lots of ways that they might have genetic heart failure. Yeah one, second there, but to answer very specific question you just asked, we did not use PAP and part of the reason we didn't use PAP is because you can see changes in the pulmonary arterial pressure associated with any one of those forms of heart failure, hardware disease will increase PAP, histophilosis in cardiac muscle will increase PAP, and also all of those diseases, over time, will result and decrease PAP it's kind of like fever right, we see the same thing and feedlot calves if we measure rectal temperatures and feedlot calves when they start to get sick their temperature goes up. And after a while their temperature comes back down, and it does it for one of two reasons, one is because they recovered or two is because they're approaching ambient temperature right there they're not with us anymore, so. You can get a lot of interesting associations that are not real by using an outcome that has a lot of different paths coming into it. So that is I think PAP, especially high elevation is a really valuable tool, I hear a lot of people talking about the value at ovation and how much good it's done for them. We were concerned in our study about the number of ways that a feedlot animal could get heart failure, and that it would it would have might not be a specific enough definition of disease to give us really clean genetic outcomes.

**Kiernan Brandt:** That was, that was a really, really good way to put that and I appreciate you putting that spin on it. So you guys ended up looking at a huge data set of feedlot calves to then go ahead and end up making pulling some out of that and making some pairwise comparisons and like with affected animals versus genetically similar non affected animals right.

**Dr. Brian VanDerLey:** Yeah, so what we did is we basically we had four cooperating feedlots that screen their cattle for cases of heart failure. When they found a case of heart failure, they would call us, we would travel out to the yard, we would euthanize that animal and do a fairly complete necropsy to make sure it actually did die from heart failure, and not one of the versions of heart failure that we're aware of. And then we would select an animal from that cases home pen that had been basically raised the same way, usually from the same source we assume from the same source. Sometimes you know the feedlot pen riders got really good at this, they would, if there was Sire identification on tags, which in some of the custom fed cattle that these yards that we went to that that did happen, they would match it on Sire at times, so at the end I don't remember the exact numbers, but basically there, we screened about 150,000 head of cattle for cases. Out of that population over about two years of time we had approximately 125 cases that we went out and necropsied and collected. We actually threw a number of those out because they didn't meet our case definition and our case definition was they had to be basically terminal congestive heart failure cases meaning if we didn't euthanize them, they were going to die shortly. And they also couldn't have any signs of the other causes of heart failure, so if they had severe chronic pneumonia we did not take them as a case if we couldn't get an adequate control for them, we didn't take him as a case. So we did cull the cases down, but we ended up with 102 pairs of cases and controls that were very closely matched but actually from fairly diverse sources. Four yards contributed cases those hundred and two cases and within those hundred and two cases, they were actually from, um I'm going to give, you guys probably have the numbers in front of you, but it was like 30 some different sources 36 I believe. I should have the numbers in front of me to you guys are making me look bad.

**Kiernan Brandt:** I think the final count was 21 genetic risk factors.

**Dr. Brian VanDerLey:** Yeah so we've so when we did the analysis we had we found 21 risk factors that met two criteria, one is they had to affect at least they had to be in play at least 25% of the case control pairs. And the second factor was a head to have an odds ratio of three, meaning that the odds of disease and the animal, with the risk factor was at least three times higher than the odds of disease and the animal that did not have it. So that's relatively, those are fairly stringent criteria that's we think it's a pretty high bar. But some of the work we're actually calling that list and that's some of the research that's going to be forthcoming here in the next couple of months will be a paper coming out. Where we actually came up with an even more stringent way to look at those numbers and further reduce the list so. The final list we have will have significantly less than 21 on it and you notice in the fact sheet that's available this is available in the US MARC website under the there's a little menu option down on the toward the bottom of the homepage where it says be bvCHF or bovine congestive heart failure. We actually really worked on two risk factors that we found so these two risk factors we call them be CHF two be CHF five they're actually associated with two genes, one of them is in a non, it's called the control region it's a non-coding RNA region. For the people out there who have some genetic background, but basically it's not the part of the DNA code that actually makes a protein or codes for protein but it's part of the code that controls, how much of that protein or how often that protein gets made. So one of the risk factors is in there and it's a gene called NF1A, and it is a there's a lot of functions that we could talk about but very generally it's kind of involved in the partner, the determination of whether stem cells turned into muscle cells or white or brown fat cells is some of the research that we've been able to find. The other pro or the other gene is called ARDC3 we call this the bCHF five. It is associated with beta agonist receptor control function and that, the risk factors actually in a gene and would actually code for a change from a think it's a tyrosine to a cysteine which would actually probably change how the protein works. So that is very likely we don't know for sure, at this point, but it's very likely to be one of those biological, uh, it is a mutation that has a biological outcome. So we're pretty excited about both of those the two of them together, increase the odds of disease 15 times over calves that have neither those two so they're both pretty big risk factors.

**Olivia Amundson:** Yeah I was looking at some of that in your proceedings paper, as well as in the fact sheet and that's a significant number, and maybe I'm getting a little bit too ahead of myself, but since you guys have been able to isolate some of these risk factors are what can a commercial cow calf producer, maybe do to decrease the incidence of some of this congestive heart failure, you know thinking down line, a little bit here.

**Dr. Brian VanDerLey:** Yeah so that's a challenging question to answer at this point for a couple of reasons, one is there's two numbers that we think are really important to measuring how well these two risk factors communicate the actual individual risk of a calf. And those two numbers are called positive predictive value and negative predictive value, so the positive predictive value is, if we find both risk factors in a calf, what is the probability that that calf actually becomes a case and that number is very low it's less than 10%. So what that means is that animals can have genetic risk but there's something else that has to happen to them and that something is we don't know what that is yet. We suspect that will be genetic environment can be weather, you know we've got a lot of ideas floating around but we don't have evidence for any of them we're working on that. The other number is positive predictive value or excuse me negative predictive value so negative predictive values if they have neither risk factor what's the probability or the risk that they will not become a case, so that they will stay healthy. I'll say it one more time because it gets a little confusing so negative predictive value is if they have neither risk factor how likely they are to stay healthy. That's a little more straightforward way to put it, that is really high, it's over 95% for these two tests, so if an animal tests negative for both risk factors more than 95% of them will never become cases. So it's actually probably closer to 98 it's a really high number.

**Olivia Amundson:** That wraps up the conversation for today. Catch the rest of this conversation on the next episode of Cattle HQ. To get access to any references talked about today, go to the SDSU Extension website and under Cattle HQ there will be episode content and show notes. Thanks for joining in today and don’t miss the conclusion of our conversation in our next episode. Thanks for tuning in and we’ll catch you next time.

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