

Flippin' the iceberg: A systems thinking approach to immunology and vaccination protocols in beef cow-calf systems

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Abstract

This paper offers a brief introduction into systems thinking and some of the basic thought processes used with this methodology. Systems thinking offers frameworks and tools that can be used to develop more effective strategies for effective change. These frameworks and tools help users recognize hidden and unintended consequences, as well as think deeper and wider about complex systems. Using bovine respiratory disease (BRD) as an example, this process will be used to study underlying factors that impact the immune system and thus contribute to BRD. This discussion should provide food for thought on areas where veterinarians can interact with producers to reduce the morbidity and mortality associated with BRD in cow-calf production systems and thus in the feedyard.

Key words: systems thinking, iceberg, husbandry

Introduction

We have all dealt with problems in production systems where we struggled to find a solution to a problem, such as respiratory disease in weaned calves. Our fixes either didn't work at all or after initially giving the appearance that they would work, backfired and did not provide the solution we were looking for. We were left looking for a long term solution and didn't know how to find it. We did not understand the entire problem. We were looking at a small piece of the pie rather than the entire pie. Systems thinking can help us understand these problems.

Discussion

Systems thinking is a problem-solving methodology that provides for the study of how systems work. It offers frameworks and tools that can be used to develop more effective strategies for effective change.¹⁸ These frameworks and tools help users recognize hidden and unintended consequences, as well as think deeper and wider about complex systems. Systems thinking is also a useful diagnostic tool in that effective treatment follows a thorough diagnosis.¹⁹ It is a disciplined approach for examining problems more completely and accurately before acting, as well as allowing better questions to be asked before reaching conclusions.

At the heart of systems thinking philosophy is the Iceberg Concept (Figure 1). The iceberg represents the problem that is being addressed and, as is typical for icebergs, only about 10% of the iceberg/problem is readily visible above the waterline. In order to correct the problem, one must understand the driving forces and pressures that exist in the 90% of the problem that is unseen (below the waterline). This requires embracing the entire problem by learning about the unseen factors through questions, and listening to learn rather than listening to react, hence, "flippin' the iceberg". These questions should be framed as "Why?" or "How come?" rather than "How to?".¹⁷

As an understanding of the unseen factors begins to develop, causal (feedback) loops can be used to map and document the problem and its cause (Figure 2). These causal loops illustrate several points about systems problems and fixes, such as:¹⁸

- The relationship between problems and their causes is indirect and not obvious.
- We create many of our own problems and have significant control or influence in solving them through changing our own behavior.
- Most quick fixes have unintended consequences and make no difference or make matters worse in the long run.
- In order to optimize the whole, we must improve relationships among the parts.
- Only a few key coordinated changes sustained over time will produce large systems change.

Characteristics of issues that systems thinking is most applicable to include:¹⁷

- The problem is chronic.
- There is a known history. Data and knowledge of the issue exists.
- Prior attempts to solve the problem have failed.
- Multiple perspectives exist on why the problem exists and what should be done.
- The belief exists that more can be learned about the issue.
- There is some control or influence over the issue, including access to key stakeholders.

As we think about chronic problems in beef production systems, bovine respiratory disease (BRD) quickly comes to mind. Morbidity and mortality associated with BRD continues to slowly increase in spite of vaccine development,

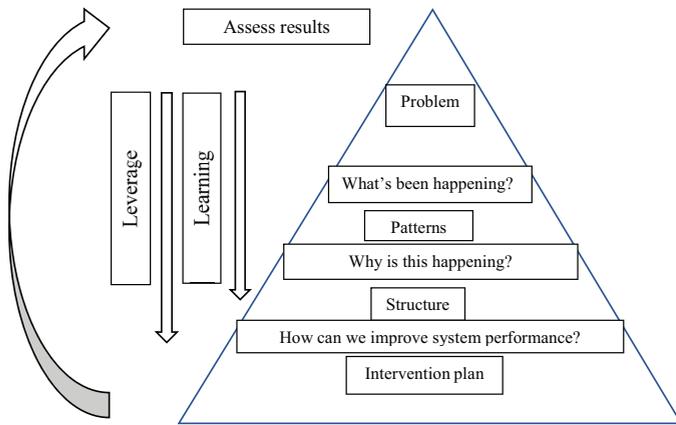


Figure 1. Steps in Systems Thinking Iceberg.¹⁷

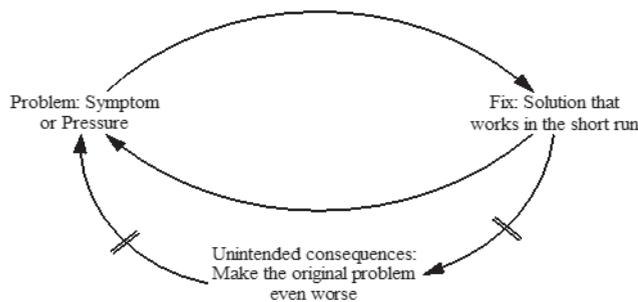


Figure 2. Unintended consequence causal loop.¹⁸

antimicrobial development, and numerous research projects. Why does this problem continue to cause the morbidity and mortality that it does? Why is the immune system of many cattle not functioning adequately to prevent BRD? The basic reason BRD continues to be a problem is that we have used linear thinking to apply quick fixes (chasing the bugs) without adequately addressing the components of the problem that are under the waterline (Figure 3).



Figure 3. Linear thinking model.¹⁷

If we flip the iceberg by embracing the problem and address components below the waterline, we can develop a causal loop model that is demonstrated in Figure 4.

This model is based on the concept that cattle develop respiratory disease for 1 of 2 reasons, either the immune system is suppressed or it becomes overwhelmed. When 1 of these 2 things happen, the bacteria that are normal inhabitants of the respiratory tract are allowed to flourish.^{24,40} Thus, these bacteria are associated with BRD, but the true cause is the factor(s) that created or influenced the immunosuppression. The case can be made that BRD is a clinical sign of underlying problems in the production system.

In order to practice good antimicrobial stewardship and reduce waste of the resources that have been entrusted to our care, we must reduce morbidity and mortality throughout the beef cattle industry. As the model suggests, basic animal husbandry practices play a significant role in determining whether a calf is immunocompetent or immunosuppressed. These practices include:

1. Nutrition
2. Shelter
3. Biosecurity
4. Colostrum
5. Genetics
6. Low-stress weaning, handling, and early-in-life castration
7. Parasite control
8. Vaccine protocol

Let's explore these practices to see how they impact the immune system and how we can use them to help producers improve morbidity and mortality caused by BRD.

Nutrition

"Because nutrition matters" Those 3 words very appropriately summarize the importance of nutrition to the lifetime health and performance of beef cattle. Gestational nutrition will serve as the foundation for this discussion as protein, energy, vitamins, and trace minerals during pregnancy are necessary on a timely basis in order for cattle to perform as expected.

Extensive fetal programming work has been done in the last 20 years demonstrating the importance of protein intake during the third trimester of pregnancy. A study at the University of Nebraska showed that the steer calves out of cows that were supplemented with protein while grazing dormant pastures outperformed steers born to unsupplemented cows in the feedyard.¹⁶ The same study demonstrated the yearling reproductive performance of heifer calves born to supplemented dams was significantly better than that of heifers whose dams were not supplemented. Two studies at New Mexico State University (NMSU) demonstrated that protein supplementation strategies during the third trimester of pregnancy impacts feedyard BRD morbidity and mortality.^{29,30} One set of cows received supplemental protein 3 times a week, another group received free-choice protein supplement, and the third received protein when inclement weather was anticipated. The trace mineral for the free-choice group was incorporated into the protein, while the other 2 sets of cows were on free-choice mineral. Figure 5 is a summary of the health performance of the steers from these studies in the feedyard.

Given the transfer of trace minerals from dam to fetus that occurs in the third trimester and the importance of this transfer to immunocompetence,^{41,42} the question that bears asking in these 2 studies should be, "Are the differences seen in these studies due to protein supplementation, trace min-

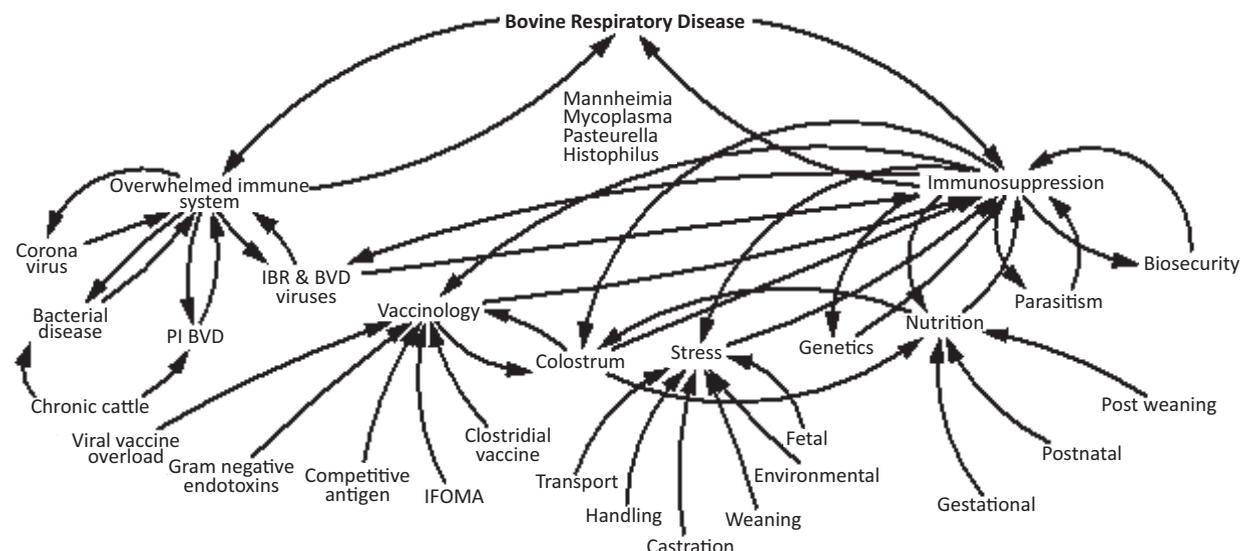


Figure 4. Bovine Respiratory Disease Causal Loop Iceberg.

		<u>3X</u>	<u>CONT</u>	<u>VAR</u>
4-year study	Morbidity %	48	16	37
	Mortality %	4.1	4.6	3.3
1-year study	Morbidity %	37	0	25
	Mortality %	16	0	0

Figure 5. Summary of New Mexico State University Studies

eral supplementation or a combination of the 2?" The cows in the free-choice protein group received both the protein and trace mineral they were supposed to since the trace mineral was incorporated into the mineral, while the cows in the other 2 groups were offered free-choice mineral.

Figure 6 shows data from a Kansas State University (KSU) anaplasmosis study looking at chlortetracycline levels in plasma.³⁴ The chlortetracycline levels on the mineral feeder group is as good an indicator as this author has seen, that not all cows consume free-choice mineral as we think they should, and thus don't all consume the trace mineral we believe they are consuming.

Considering the NMSU and KSU studies in light of the following statement, forced intake of trace mineral certainly makes sense. "Greatly overlooked in the cattle industry are the opportunities to add these minerals, trace minerals, and vitamins in grain or protein mixes being fed to the cattle during the winter months. Since one of the most critical times that these nutrients be supplied is 30 to 50 days pre-calving and through the breeding season, the concept of force feeding has considerable merit in the industry both from an efficacious and economical standpoint."⁸

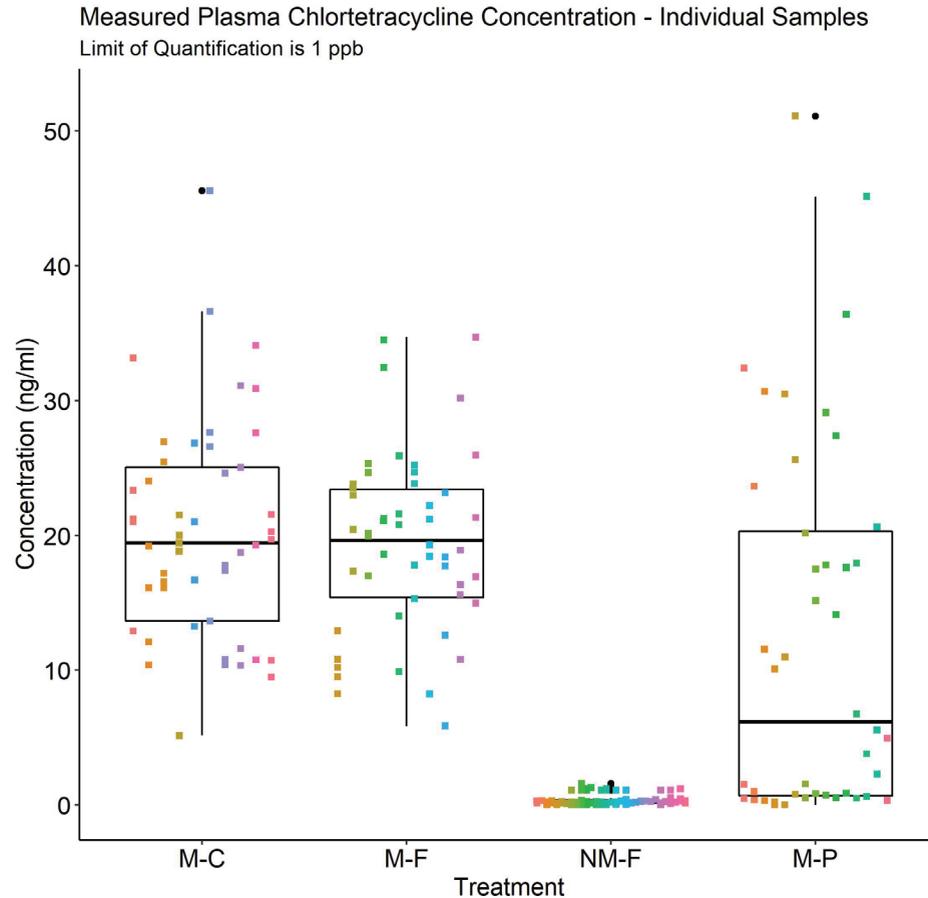
Another interesting fetal programming concept is found in a University of Idaho study looking at Weak Calf Syndrome.²

In this study, half of a group of two-year-old heifers were fed supplemental protein in the third trimester, while the other half was not. Calves were not allowed to nurse their dams until after they had been tube fed a standardized colostrum. The calves from the supplemented heifers absorbed significantly more colostrum than the calves whose dams were not protein supplemented.

As we think about energy in the pregnant cow, it is essential that the cows are maintained in a near optimal body condition score (BCS), 5-5.5 for cows and 5.5-6 for heifers, as they go into calving. These condition scores indicate that the dams have adequate energy intake during gestation. Cows whose energy is restricted in late gestation tend to give birth to calves with light birth weight, as well as low vigor and ability to survive.⁸ These calves are more susceptible to neonatal scours and have a higher mortality from birth to slaughter. In another study, calves born to thin cows are slower to nurse, have lower IgG and IgM levels, and reduced thermogenesis.⁷ Cows that are in adequate BCS going into calving have the necessary brown fat in the colostrum to serve as a neonatal energy source, and will have the necessary condition for rebreeding in a timely manner.

The levels of trace minerals fed during gestation do not have the impact on calf vigor that protein and energy do.⁷ However, there is evidence that the trace minerals will impact immune system function.²⁷ Copper, zinc, and selenium are the primary trace minerals of interest when immune function is discussed. When reproduction is considered, manganese should be evaluated. Trace minerals are transferred from the dam to the fetus during late gestation to provide the very high fetal liver stores of trace minerals that are required for proper immune function the first 50 to 60 days of life.

Figure 7 shows the effects of trace mineral levels as these levels drop from optimum to overt signs of deficiency.



Points in the same vertical plane represent the same individual animal.

Figure 6. Kansas State University Anaplasmosis Study (chlortetracycline levels)³⁴. M-C: Chlortetracycline (CTC) was administered via oral bolus. M-F: CTC was delivered via dried distillers grain. M-P: CTC was delivered in loose mineral offered in mineral feeder. NM-F: CTC was not offered to these animals.

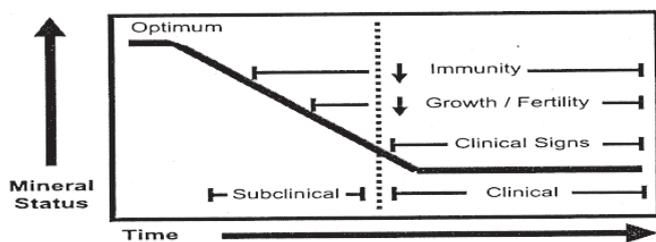


Figure 7. Effects of trace mineral levels in cattle.⁴⁴

It should be noted that the immune effects are the first to occur, followed by growth and fertility effects. These effects occur well ahead of the signs of overt deficiency, such as the appearance of red hair in black cattle that occurs with copper deficiency.

Nutrition is of primary importance as we discuss the impact of animal husbandry practices on the immune system function in cow-calf systems. Whether it be gestational

nutrition to ensure a healthy calf born, postnatal nutrition to ensure that the cow will milk adequately as well as rebreed, or the effect of nutrition on colostrum quality and quantity, adequate protein, energy, trace minerals and vitamins are essential.

Colostrum

Completion of passive transfer of maternal immunity to the calf through colostrum is an important factor in determining the preweaning health and performance of beef calves.⁴⁶ Calves not receiving adequate IgG through colostrum have been shown to have increased odds of pre-weaning mortality (odds ratio [OR]=5.4), neonatal morbidity (OR=6.4), and preweaning morbidity (OR=3.2), compared with calves receiving adequate IgG when measured at 24 hours of age.⁴⁶ Calves suffering morbidity during the first 28 days of life had a 35.2 lb (16 kg) lower weaning weight compared to non-morbid calves.⁴⁶ This study observed that calves with adequate plasma protein at 24 hours of age had decreased odds of morbidity

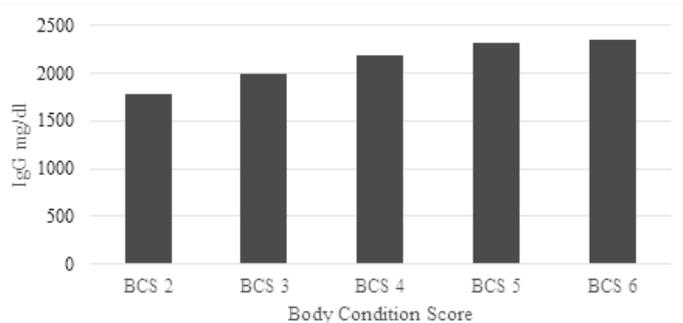


Figure 8. Effect of Body Condition Score on serum IgG levels of calves.³¹

(OR=3.0) and respiratory tract morbidity (OR=3.1) during the feedyard production segment, compared with calves not having adequate plasma protein. Another study reported that lower perinatal IgG1 concentrations were associated with higher morbidity rates, higher mortality rates, and lower average daily gain prior to weaning.¹² Calves with serum IgG1 concentrations <2,400 mg/dL were found to be 1.6 times as likely to have a morbidity event and 2.7 times as likely to have a mortality event before weaning as calves with higher IgG1 concentrations. Calves with serum IgG1 concentrations greater than or equal to 2700 mg/dL were found to be 7.3 lb (3.35 kg) heavier at 205 days of age than calves with lower IgG1 concentrations. There were no significant associations found of serum IgG1 concentrations with feedyard morbidity, mortality, or average daily gain in this study.

Fat and leukocytes (primarily lymphocytes) are other components of colostrum that are essential for the neonate. Colostral fat serves as a nutritional energy source to help the neonate maintain thermostability, especially in the first hours after birth. Colostrum plays an integral role in supplying neonatal energy needs and this role has been described to be of equal importance to colostrum's role in transferring passive immunity to the newborn.⁴ Calves born to prepartum protein-restricted 2-year-old beef heifers had lower heat production as a neonate than calves from heifers fed adequate protein prepartum.³¹ In a related study, body condition score (BCS) of 2-year-old heifers was directly related to immunoglobulin absorption by their calves.³¹ In this study, higher immunoglobulin concentrations were thought to be due to increased immunoglobulin production of the heifer or increased calf vigor.

A possible link between these 2 studies could be that adequate protein levels in prepartum heifer diets improve colostrum immunoglobulin production as well as having a positive impact on heifer BCS. The increased body fat associated with the higher BCS could indicate increased colostrum fat content, allowing for better neonatal thermoregulation. Reduction of cold stress could improve immunoglobulin absorption by the neonate. Colostral leukocytes are absorbed by the neonatal gastrointestinal tract and can influence the immune function of the calf.³² The impact on neonatal morbidity and mortality associated with this leukocyte absorption

has not been studied. However, one could hypothesize that if the lymphocytes of the dam are primed with viral vaccine antigens prior to colostrogenesis, the viral immunity of the calf could be enhanced early in life by the colostrum lymphocytes.

Calves are born with very low vitamin A and vitamin E, and thus rely on colostrum as the primary source of these fat soluble vitamins. Both of these vitamins are necessary for optimum immune function as well as other tissue functions. Vitamin A deficiency has been shown to impair the viral immune response in neonatal calves.²⁸ One major role of vitamin A is its association with maintenance of the mucous membranes of the respiratory and gastrointestinal tracts. Deficiency of this vitamin causes damage to the epithelium and allows viruses and bacteria to invade.³ Vitamin A deficiency has become more prevalent in recent years, primarily due to a fire in Germany that destroyed the only plant that manufactures feed grade vitamin A, the increased use of distillers grain that is relatively low in Vitamin A content, and ongoing droughts which affect forage quality.

A closing thought on colostrum management is a suggestion to encourage producers to, if at all possible, wait until the newborn calf is dry before tagging, weighing or giving vaccines. This allows for better bonding between the dam and the neonate, which in turn encourages improved intake of colostrum. Discussions about colostrum focus on immunoglobulin transfer that occurs, but it is essential that fat content, vitamin content, and leukocyte content are considered as well.

Low Stress Handling, Weaning and Early-in-life Castration

Cattle experience a number of environmental, managerial, and nutritional stressors that create immunosuppression, thus impacting productivity, health and well-being.³ Weaning, castration, commingling, handling, and transportation are the stressors most commonly discussed. Environmental, nutritional, and fetal stressors are of equal importance and bear inclusion in the discussion.

Castration on arrival at the feedyard has been shown to reduce feed and water intake, increase morbidity and mortality, and decrease average daily gain when compared to animals previously castrated.¹¹ It is the opinion of this author that castration is a low-hanging fruit that could be dealt with prior to weaning and have a significant impact on morbidity, mortality and subsequently, antibiotic use.

Fetal stress is of particular interest due to its effect on lifetime health and performance. Studies have shown that fetal stress impacts organogenesis, which at least in part explains the impact on health and performance, but also makes one speculate whether it plays a role in conditions such as brisket disease in feedyard cattle.^{13,22,25}

We must continue to strive to reduce stress at the cow-calf level of the industry. There are still far too many instances of calves being abruptly weaned, transported, commingled, and castrated within a matter of a few days. We can do better.

Parasitology

Studies assessing the effect of deworming on health performance of calves seem to yield mixed results. One study observed that deworming had no effect on antibody response to vaccination or infectious bovine rhinotracheitis virus challenge.³⁵ Another study stated that health and growth performance of calves may be adversely affected by vaccination, high fecal egg count and fever on arrival, yet found that the effect of deworming on health or performance was neither positive or negative.²¹ A review article cited one study that showed a negative effect to deworming in the first 2 weeks after feedyard arrival and another that showed dewormed, preconditioned calves had a lower disease incidence when compared to calves that were not preconditioned or dewormed.³⁹

It is the clinical observation of this author that deworming calves at the time of preweaning vaccination with an injectable avermectin seems to reduce postweaning morbidity. The hypothesis is that reducing the parasite burden improves serum protein, thus allowing a better immune response.

Vaccinology

The initial consideration in our vaccinology discussion is how we create active immunity in the face of maternal antibody (IFOMA) that is present in the young, nursing calf. Our cow vaccination protocols should be providing adequate antibody to provide immunity for the neonatal calf, assuming that our protein, energy, and trace mineral nutrition is right and has given the cow all of the tools she needs to produce antibody and that adequate passive transfer occurred. It seems ironic that we work hard to get adequate antibody into the neonatal calf, then that same antibody interferes when we try to create active immunity.

The probability of seroconversion following parenteral vaccination in calves with high maternal antibody levels is low.⁴⁵ While the probability of these calves seroconverting is low, there is ample evidence that parenteral vaccination, both MLV and killed virus (KV) vaccination, will prime the immune system IFOMA to allow for an anamnestic response.^{1,6,47} It should also be noted that the response to KV vaccine is variable.⁵ It should be noted that the anamnestic response to bovine respiratory syncytial virus vaccine is the weak link with the parenteral vaccines.

Both types of parenteral vaccines will stimulate T lymphocyte production IFOMA which primes the immune system to provide bovine virus diarrhea viral protection following booster vaccination.^{1,5,6,15,47}

Intranasal (IN) vaccination seems to offer several unique features when used IFOMA. Not only is interferon produced, but secretory antibody (IgA) is produced. The immunity that is produced when IN vaccines are used is sufficient to provide an anamnestic response to infectious bovine rhinotracheitis virus (IBR) and BRSV as well.^{14,23,26}

Another advantage of IN is that the competitive antigen phenomenon that is occasionally seen with the use of parenteral MLV vaccines is avoided.⁹ This phenomenon can occur when MLV vaccines are used in IBR naïve cattle concurrently with other vaccines, and the IBR vaccine inhibits the immune response to the other vaccine.^{10,20,37} By utilizing the mucosal immune system to prime against IBR virus, this phenomenon is avoided.

Endotoxins associated with some vaccines are known to have a negative impact on immune response and animal health.³³ These endotoxins are usually associated with gram-negative vaccines, such as scour vaccines containing whole cell *E. coli*, *Histophilus* bacterins, pinkeye bacterins and some respiratory bacterins, although they can be found in other vaccines. Mishandling of gram-negative vaccines can exacerbate this issue. As a general rule, do not administer 2 or more gram-negative vaccines concurrently.

Inflammation associated with the use of clostridial vaccines has been reported.^{36,38} The most common change associated is a reduction in feed intake. Inflammation-related biochemical changes are also observed. Given that these changes impact immune function, consideration should be given to the timing of clostridial vaccination associated with weaning.

Another clinical observation by this author is that the concurrent use of modified-live virus (MLV) intranasal vaccine and a parenteral MLV vaccine has a negative impact on stressed calves, such as abrupt-weaned calves or transported calves. In discussions with immunologists and technical service veterinarians, it seems they believe this is real. The hypothesis is that proinflammatory cytokines are produced when this much MLV vaccine is given to stressed calves. The hypothesis can also be made that the same phenomenon occurs when calves are revaccinated with MLV vaccines shortly after the initial vaccination with MLV vaccine. A review of the records on 85 sets of backgrounded calves over a 5 year period of time revealed that calves given a booster vaccination less than 14 days after the primary vaccination had a 29.8% morbidity compared to a 10.6% morbidity in the calves boosted 14-28 days after the initial vaccination and a 12.3% morbidity when the booster was given more than 28 days following the first vaccination.⁴³

There are a number of considerations as one puts together vaccination protocols for cow-calf enterprises. Among these are the vaccination history of the cows, maternal antibody, and interactions between various antigens being used while addressing disease issues present in the herd. Strive to keep these protocols simple, yet effective.

Sample Protocols

Spring: Calves

IN IBR-BRSV-PI3

2 mL in one nostril
(change cannulas each calf)

BVD/ <i>Mannheimia</i>	2 mL SQ neck
Clostridial	7 or 9-way
	2 mL SQ neck
Pinkeye (optional)	2 mL SQ neck
Castration	
Implant (steers only)	
<i>Spring: Cows</i>	
Pinkeye (optional)	2 mL SQ neck
Benzimidazole dewormer	
Permethrin pour-on w/ larvicide	
<i>Spring: 2-year-old Heifers</i>	
MLV FP 5-way viral L5	2 mL IM neck
<i>Campylobacter</i>	2 mL SQ neck
Pinkeye	2 mL SQ neck
Benzimidazole dewormer	
Permethrin pour-on w/ larvicide	30 mL topical
<i>Spring: Herd Bulls</i>	
Breeding Soundness Exam	
Temp Sensitive viral w/ KBVD-L5	5 mL SQ neck
<i>Campylobacter</i>	2 mL SQ neck
Benzimidazole dewormer	
Permethrin pour-on w/ larvicide	
<i>Fall: Calves Prewean</i>	
MLV 5-way viral w/ <i>Mannheimia</i>	2 mL SQ neck
Avermectin injectable	1 mL /110 lb SQ neck
Permethrin pour-on w/ larvicide	
<i>Fall: Calves Wean</i>	
MLV 5-way viral	2 mL SQ neck
Clostridial 7-way	2 mL SQ neck
<i>Fall/Winter: Cows</i>	
Preg check/BCS	
Temp Sensitive viral w/KBVD-L5	5 mL SQ neck
<i>Campylobacter</i>	2 mL SQ neck
<i>E. coli</i> , Rota, Corona C&D	2 mL SQ neck
Avermectin pour-on	4.5 mL /100 lb topical
<i>Fall/Winter: Herd bulls</i>	
Avermectin pour-on	4.5 mL /100 lb topical
<i>Fall/Winter: Purchased bred heifers</i>	
Temp Sensitive viral w/KBVD-L5	5 mL SQ neck
<i>E. coli</i> , Rota, Corona C&D	2 mL SQ neck
Injec. Trace mineral	4 mL SQ neck
Avermectin pour-on	4.5 mL /100 lb topical

Conclusion

“Cattle simply need stronger immunity at the time they leave their farm or ranch of origin, and

this problem is more about producer education and implementation than it is about technology or know-how.” Tom Brink, Beef Improvement Federation, 2016

All of us associated with the cow-calf segment of the beef industry should pause and ask what we could do differently to improve immune function in cattle arriving in the feedyard.

Systems thinking allows us to embrace and understand the 90% of a problem that is below the waterline. This “flip-pin’ of the iceberg” provides details that we miss when we focus on the 10% that is above the waterline. The BRD example that we used should give you an understanding of the details that are missed when the focus is on bugs and drugs. Hopefully, it will help you enhance the manner in which you work within production systems you are associated with and improve immune function in cattle arriving in the feedyard.

In conclusion, I challenge each of you to learn to look at the entire system. Ask numerous questions. Listen to understand rather than listening to respond. Look for the arrow and the measuring spoon in the Fed Ex logo (look for the small details).

Build relationships by building trust. Show people that you care. People don’t care what you know until they know how much you care.

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