Feedlot Section

A Review of the Etiological Factors Associated With the Bovine Respiratory System

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Like all researchers I have certain biases. I'm biased towards the organisms I work with and becaue I wasn't here to join in the BVD festivities yesterday, I will try to rebutt a little bit and point out that maybe there is something besides BVD causing respiratory disease or predisposition to bacterial pneumonias. Let us go down the list of infectious agents of bovine respiratory disease. Many people feel that *bacteria* are probably the things that make all the other ones important because maybe without bacteria we would not end up with pneumonias that kill animals or make them do poorly for life. But, maybe without the *viruses* we would not have the predisposition or a lot of the predisposition that allow the bacteria to get where they can do that kind of damge. *Mycoplasmas* and on down the list, a big question mark in many ways and yet we'll talk about those at greater length later on. I've left the *protozoa* off this list. I don't know that there is any solid evidence that the one protozoan frequently isolated from lung is of any economic importance and I do not include parasites here because I don't know much about them.

Most people agreed that pasteurella are probably the most important bacteria in bovine respiratory disease but not everybody agreed on which of the two species, *Pasteurella multocida* or *Pasteurella hemolytica* is the more important but let us say that pasteurella are important. Hemophilus is probably next in importance and then of course some of the others like Corynebacteria and Salmonella which are a problem or else predispose less frequently. I have listed some viruses which we work with in cattle respiratory diseases and some which have been worked with very little. Leading the list IBR, which we know to be an important pathogen, PI3 of course the old "grand daddy" of shipping fever and bovine respiratory disease, the one that has been worked with the longest and certainly many people feel are of not too much importance and yet there are others who feel they are quite important. Then BVD and I won't say a thing about that because you know more about it than I do since many of you I assumed were at yesterday's meeting. the next one a lot of you maybe have not heard of, BRSV which stands for bovine respiratory syncytial virus, happens to be one of the ones I'm working with. A blue tongue virus I had to list. Certainly it's important in differential diagnosis and often times what is called BVD turns out to be blue tongue and maybe of some importance in the respiratory disease complex but certainly of importance from the standpoint of differential diagnosis from BVD. As we go down the list for most of our evidence of the importance of the other viruses we have to lean on workers from other countries. Some work has been done certainly with adenoviruses both at Oregon State, Maryland and Iowa State. We do a little at Lincoln and a lot more needs to be done with those viruses to determine how important they are in the respiratory disease complex. The same with rhino viruses. It has been shown at Missouri and by some others that you can get disease in experimental calves with rhino viruses but how often they are involved we don't know until a lot more serology and experimental infection work is done. Reo viruses; very little work has been done in this country with these viruses in cattle and the same for enteroviruses as far as respiratory disease pathology is concerned. There are others that could be added to the list and there are other herpes viruses like the DN599 which we hear about from time to time, malignant catarrhal fever, some others which we could add but since I'm ignorant of those subjects entirely, we will just lump those and call them others.

I do want to get you thinking in terms of the three lines of defence and particularly the nonspecific types of defence against respiratory disease. They are all very important in

resistance to respiratory disease and of course the first line of defense is what keeps most of us from dying rather early in life. There are many viruses which human beings are not susceptible to, the same with cattle. There are many viruses which they are not susceptible to and that would be a species resistance. There are some respiratory diseases which spread to the respiratory tract from a generalized infection and intact vascular endothelium would be part of the line of defense against that type of infection. Lack of cell service receptors, that again is just species resistance and yet within species there are some differences, individual differences and this is an area of nonspecific resistance which has been greatly understudied in the past and is an area that we have neglected. The natural inhibitors in blood and other body fluids are also part of the first line of defense. This first line of defense is that defense which is intact in the normal animal at the time of infection. The second line of defense is that which is called into play very early in a virus disease, for instance, interferon production which takes place in the first 24-72 hours depending on whom you are talking to or what virus you are talking about and that's nonspecific in that it will protect, not only against the virus that caused the cell to produce the interferon, but also against some other viruses if not all other viruses as well. An elevated body temperature in response to a virus infection is certainly an area for argument but thought by many to be of considerable importance in overthrowing a viral infection. Changes in pH and oxygen tension in the area of infection sometimes lead to a creation of a less satisfactory environment for that agent or possibly a more satisfactory environment for a secondary agent. The third line of defense, the one which most of us are talking about when we refer to resistance to respiratory disease is humoral and cell mediated immunity, good old syringe and needle immunity and the immunity which comes with recovery from a disease.

Environmental factors are something else which we talk about a lot but which have been studied far too little and we can list them; *temperature*, many of us have the impression that considerable changes in temperature on the order of 40 degrees or more are important in predisposing cattle to respiratory disease, and yet very little has been done to prove this. *Humidity,* we know that certain types of infections, particularly some mycoplasma infections in other species are affected greatly by humidity. We know considerably less about conditions in cattle. Precipitation obviously would be tied in with temperature as far as the creation of a state of stress, and more susceptible to infection with the various agents. It has been shown that barometric pressure and electrostatic charge can have considerable effect on the onset of disease or the feeling of well being among animals, something which years ago we tried to study a little bit in turkeys and found certainly that we could see patterns but we could not really create the experimental conditions very easily to try to recreate the natural conditions. There is not a large animal practitioner alive, I'm sure, who has been in practice many years who does not go out some days and say that this is the kind of day that I see more milk fevers or this is the kind of day that cows or horses or any kind of animal might come down with certain types of diseases more commonly or cows might calve more commonly. So we all have our impressions that they are important but we don't really have anything that we can pin down as being concrete. Gases certainly irritate and allow for increased invasion of mucous membranes and particulate material create blockade of the clearance of mechanism cells creating a conditions at least in experimenal studies where phagocytosis of invading microbes is considerably reduced.

There are sources of physiological stress associated with all kinds of marketing calves. We can run through them very quickly. Weaning has many effects on a calf obviously. Certainly a feed change and a decrease in consumption of the best feed for a calf and not to mention the psychic effects of weaning. Vaccination, dehorning, branding, castration, dust are other examples. A lot of people think that dust does predisponse to respiratory disease from an experimental standpoint. Enough dust will do the same thing that other particles will do in causing a blockade of the cell clearance mechanisms, but there are others who say that the dust doesn't really bother calves and we have worked in pretty dusty conditions and it does not seem to calves at least if they are healthy otherwise. So there is an argument there but if there is enough dust, I'm sure it is bound to increase susceptibility. Some of the things include noise, crowding, and social stress from being thrown with new calves. Certainly these are psychic effects which we probably underestimate as far as the effect on a calf and the effect on its resistance to infection. Physical abuse associated with many of these things also would have a psychic effect and is probably more important that we give it credit for.

If we were to list one thing in cattle respiratory disease that has to be the most important it is shipping and the resulting *fatigue*, which is very important in setting up a calf for infection, increased susceptibility to infection. *Exposure* is also important. *Starvation* obviously has quite an effect on the physiology of the animal, while it sometimes may increase their susceptibility at other times it may decrease it. We don't really know because it has been studied so little. *Dehydration* certainly has an effect on the ciliated mucous membranes and decreases the effectiveness of the ciliary clearance elevator, not to mention the physiological effects associated with dehydration. *Gases and particles,* in this case being due to diesal fumes from the trucks primarily, are important. *Worming* is something we hear more and more about these days, the effects of worms and worming. I think certainly the effects or rather the importance of lungworms in setting up the lungs for pneumonia has not been studied enough and I can remember when I was in Oklahoma a few years back talking with several small feeders who felt that when they put their calves on a worming program, they decreased their respiratory disease considerably and yet the things that have happened or that we have learned about some of the common worming agents since then might lead

us to think that could have been one of two things, either they were getting rid of worms and had a worm burden which contributed to their susceptibility to infectious disease before they started on a worming program, or perhaps the wormers that they were using were some of the ones which cause immunomodulation. Some of them, such as levamisol, would be a good example which might stimulate immunity in some ways. So they could have an effect on the immune system as well as on the worm burden which brings us around to the subject of preconditioning and how to avoid the stresses that we've just been talking about.

Preconditioning is something which waxes and wanes in its popularity and depending on the area that you are from, you hear more or less about it now than you did some years back. There's no question but it can be helpful and yet it is used probably less now than it was a few years ago. Does it work? Yes, it obviously does work in some cases and if so why isn't it used more? Well, apparently the cost-benefit ratio is such that people are willing in the majority of cases to try their luck without it and if not, why not? This might be a good time to talk a little bit about gambling and moving cattle and certainly the people that buy cattle which have been shipped great distances, 1500-2000 miles or even several miles only, may be said to be asking for a little respiratory disease and presumably they are gambling and willing to take that risk. The ones that I really feel sorry for are those who made contact with the cow-calf operation, say in the same state or in a neighboring state may be a 100-200 miles away at maximum or maybe 4-500 miles away, but still close enough so that they can get them there in one day, easily in daylight hours even. They make contact with those people, get them to precondition the calves, do everything possible, even use their own truck or rent a truck and do their own cleaning, go get those calves, take them to their own place, their own feedlot without ever moving them through a sales yard and then have a wreck. And those are the ones that I really feel sorry for and I think that if we find ways to help them we will be finding ways to help everybody and maybe we can find ways to make preconditioning more acceptable from an economic standpoint and more widely used. Successful preconditioning, of course, first of all means preventing exposure to dangerous pathogens until they are immunized. That means vaccinating them against such things as IBR, and if you consider BVD to be important, against BVD, if you consider PI3 to be important, against that one while they are still on the cow and giving them at least a couple of weeks before they are exposed to other calves. In this way you hope to slow down the exposure to agents, certainly exposing them to only the milder pathogenic organisms than when they are mixed with other cattle and presumably the desirable effect from preconditioning and then moving them through as few feedlots as possible.

Presumably any desirable effect is due to simply a slowed down exposure to organisms which might otherwise be additive or synergistic in their action and I am firmly convinced that the average calf can handle almost any infectious agent if it is exposed to them one at a time, but it is when they're exposed to several of these agents that they sometimes get sick even though there is little stress associated with their movement or little perceptible stress. Recent work in England, was reported by Andreas at a bull testing station, and any of you who have worked with those kinds of stations know that they are a cesspool for respiratory disease. Agent activity involved two groups, handled singly that arrived at the station at 7 months of age where the calves were penned singly and kept until they were 13 months of age. Only one in eight had to be treated. Then they changed their method of handling calves and started putting them in large groups at 6-9 months old on arrival and then singly at 9-13 months old on arrival and 1 in 2 of those animals had to be treated. Then they compromised and put them in groups of 2-3 from 6-7 months of age arrival for one month and then into larger groups from 7-10 months and then singly. Less than one in three of those had to be treated. They thought there was something worth following up and they are going to do more studies to see if maybe they could determine a method of handling which would not be too expensive, but still would hold respiratory disease and the cost of treatment to a minimum.

How do you go about studying these additive infections, these combination infections? How do you approach the problem and what do you hope to find out with experimental calves? I think we have to start there and the first thing to do is find out if an agent will infect a calf which is wide open to respiratory disease and then take it from there into other experiments, preferably field experiments. Some calves were taken by caesarean section, put into an isolator for a month and then raised in strict isolation. We wear rainsuits and shower about three times before we get in where the calves are, and wear face masks to prevent any exchange of organisms between the handlers and the calves and we are raising these particular calves in pairs. We have a new building which is a beautiful facility. Before surgery we put a bubble on the cow. The calf goes into the metal isolator and he is kept there for 4-5 weeks. If we want to keep them that long they have to be kept in one of the isolation pens. How do we hope to find out anything with these caesarean derived, colostrum deprived calves? I think we can be criticized for doing our work in those kinds of calves but I think that is step #1. The other means that we use to study respiratory disease in our work are epidemiologic surveys of cattle at the Meat Animal Research Center at Clay Center. It is a fantastic facility and certainly a great place for us to work with cattle which are raised under near ideal conditions. Not a lot of hills around there, but plenty of acres of grass and crop land and they have just about every kind of genetic pool and just about every kind of cross that you can imagine at the station. They have about 6,000 cows that they calve out each year and they raise the calves and feed them out themselves. The facilities for handling the cattle are quite good, complete with an inside chute area where we can bleed and take nasal

swabs and get all the help that we want at the same time. What are we finding out in such plush surroundings? Among other things we are finding that they get good response to IBR, PI3, BVD vaccine and we have found some adenovirus serum conversions but I am going to dwell on today with antibodies to bovine respiratory syncytial virus and the calves at the research center each year go through a syndrome which for want of a better term is often called "adenomatosis—emphysema complex". We have tried for the two years that I have been there to isolate an infectious agent from it. We have not been successful and so we are looking in looking at those agents which are hard to isolate, which we isolated from calves a number of years earlier at Iowa State and seemed to be a good candidate and that was the respiratory syncytial virus which has also been worked with by people in Europe for a good many years. Sure enough when Dr. Mark looked at serology to that virus from the 1977-78 season he found that in September and October there were no antibodies in 21 head of cattle in a high incidence line of Herefords which they have. In November, 21 of 21 were positive with immuno antibody titer which was fairly high and then that tapered off until March when 20 of 21 were positive at a much lower level. We saw the same thing in the ones from this year. I'm not saying Herfords are the only ones that are highly susceptible but certainly they are the ones in which we see the clinical signs and probably first maybe most severe but there are other breeds which are susceptible. It is an interesting virus in that it does seem to affect some breeds considerably more than others and it does point out the importance of further study on breed susceptibility to various infectious agents. In september and October there were no antibodies. In November and December, 17 of 17 and then 12 of 12 tested positive and it again continued down until April when they were last tested. The same with 10 head of Red Polls and in a pen of cross bred combinations. Lower titer certainly, but going from all negative to all positive. One group of Herefords were positive in September and October and then gradually tapered off. Maybe this is a bunch that were carrying the infection which then spread from pen to pen and went across nearly every pen in the area of the center. Probably some of you have not heard of this virus so maybe I should introduce you to it a little more formally. It is a mixo-virus and closely realated to the respiratory syncytial virus of human beings. It is not a relative of what has come to be called bovine syncytial virus but an entirely different virus. We don't really know the significance of it and we are hoping to find the significance of bovine respiratory syncytial virus. Most of the work to date has been done in Europe with experimental infection. We have done a little bit and a few other people have done some in this country but most of it has been in Europe, aside from serological studies which have been done at 4 or 5 locations in the United States and ther's no question but that it is very widespread in cattle on the order of PI3. I mention very briefly the lesions associated with the infection in cattle in the Netherlands and in Belgium. The mortality is up to 20%. There may be none but it may be as high as 20%. The acute onset is almost reminiscent of the writeups of swine influenze where the herd is almost all affected at one time it seems like. They start coughing and they show some conjunctivitis and watering of the eyes. Some have fevers. These fevers may be as high in some calves as 108 degrees or 109 degrees. There is usually, or at least in some animals, a systemic disease in the reports from the Netherlands, including loss of appetite, increased respiration rate and continued fever with an ever increasing coughing and then reddening of the nasal mucosa and some nasal discharge. The disease seems to go either of two ways. They usually treat very early and sometimes there is rapid improvement with no further signs or in other animals there may be severe emphysema which may go into chronic case or may result in acute death. In the Dutch report the lungs were heavy and large but appeared to collapse, there were a few bullae and occasionally extensive lung breakdown with grey and red lobules on the cut surface, variegated colors. Yet the reports from Belgium were apparently dealing with cattle which are more highly susceptible to the disease. There does appear to be more emphysema in the animals. The other differences are that there is a higher mortality, sometimes as high as 50%, but sometimes quite low, one or two animals out of say 100 or so. Otherwise their descriptions are fairly similar. We have infected a few calves at Lincoln and found that with respiratory syncytial virus there certainly should be an opportunity for predisposition to almost any other infectious agent which comes along. We saw some sticking together of the cilia in the bronchiole and some increase of goblet cells and in the trachea evidence of complete deciliation. We'll see this a little more dramatically in more severe animals. The turbinates in a mildly infected animal are pretty normal as far as the ciliated epithelium is concerned but with a lot of cellular material and frothy material in the lumen. In more severely affected animals, the turbinates have completely disappeared. There are many, many goblet cells and there are abnormal masses of cilia which are stuck together. The trachea of an infected animal which had severe clinical signs was completely without normal cilia and many areas which were completely denuded except for the microvilli. There were a few areas with remnants of the cilia in the trachea. This certainly gives plenty of opportunity for secondary invaders even if the primary disease was not making them ill.

I have worked with respiratory disease for a long time mostly with mycoplasmas. I do want to mention 3 species of mycoplasmas that we will probably be hearing more about in bovine respiratory disease. *Mycoplasma bovis*, which has been called *mycoplasma agalactiae variety bovis* in the past, *mycoplasma dispar* and then the urea plasma species or T strain mycoplasmas. Some work has been done in England demonstrating the importance of these mycoplasmas in coughing pneumonia and certainly they have done a lot

more to demonstrate their importance than we have in this country, but perhaps over the next year or two we will be able to do some catching up because there are several stations in this country where work is being done with mycoplasmas in cattle respiratory disease. Some of the ways that mycoplasmas could possibly cause respiratory disease are certainly the close association with the cell sometimes appears to lead to a toxic effect which is not associated with a toxin but simply with the whole organism itself. Then there are exotoxins produced by some mycoplasmas and certainly metabolites produced by some mycoplasmas which, because of the close association with the cell, cause cellular-changes and breakdown with interference with wholesale nutrition. There is competition for certain nutriments. There could also be a change in antigenicity which would lead to immune response which could cause lesions. Most importantly, I want to point out today the immune suppression which has been proven with mycoplasmas from other host species but among those from cattle only with *mycoplasma bovis.* Certainly it is an important immuno-suppressant of the cellular immune system in cattle. This work has been shown most clearly at California and I think it is something which we will be hearing a lot more about as far as the possible predisposition by mycoplasmas to bovine respiratory disease. We wonder sometimes why in experimental infections we don't see a disease which looks like what we call a mycoplasma infection in cattle. We feel, though, because there is an increase in mycoplasma antibodies, that there is a good chance that they are involved and certainly because we see respiratory disease go into arthritis from which we can isolate mycoplasma that they probably are involved and then certainly Dr. Hjerpe among others has shown that antibiotics such as tylosin which are quite effective against mycoplasmas are not effective against pasteurella and are effective in at least 40% of shipping fevers. He attributes that probably to their mycoplasma cytal activity. We also know from analogy to other host species that they are quite likely of importance.

Discussion

Question: Have these fat cattle, that you just showed a picture of, that are showing atypical interstitial pneumonia, have those animals been on Rumensin?

Answer: No.

Question: If you are involved in a problem with atypical interstitial pneumonia and there happen to be three or four animals showing signs at the same time, different degrees--some rather severe and some milder--is there anything that you could do to help in treating these or to tell the owner?

Answer: I think it's best to prepare the owner for the worst. First say that the three or four animals all might die, certainly the more severely will and that he may want to consider slaughtering the one or two that are worse and if he'd like to chance treating the less severe ones, while there is no specific treatment, you could try dexmethazone and antibiotics, as a treatment for this. I had one animal that I thought was going to die that I gave very large doses of Vitamin C, and it recovered.

Question: These animals had been on alfalfa hay, would it be a good idea to change the feed?

Answer: Probably it would be a good idea to change feed, even if it meant buying some different hay. I would suggest changing the hay for a few days anyway.

Question: Could you slaughter these at the regular packing plant?

Answer: I think perhaps with the veterinary inspection there they might not comprehend what this type of pneumonia is and may condemn it ante-mortem. So better to slaughter it privately.

Question: A large number of cattle in the west are vaccinated for lepto, what is the justification?

Answer: There were some clinical cases of lepto in South Texas this year, more than they had seen in some time, testimonials from oldtime practitioners state that lepto is a significant problem and can be a severe clinical disease in unprotected cattle. Probably, *lepto. pomona* and *grippotyphosa.* Vaccination does prevent this and as a testimony to the merits of vaccination, we don't see clinical lepto to any great extent in cattle. In dairy herds, lepto can be a fertility problem. We have diagnosed *lepto hardjo* infection in some dairy herds in our area, characterized by infertility, not by outright abortions. Febrile response with some clinical illness, some anorexia and infertility problems in the herd in general which did respond to vaccination. Confirmed by titer rises between acute and convalescent samples in the clinically affected animal.

Question: Is there any difference histologically between these three different types of interstitial pneumonia?

Answer: I think there is but I'm not a histopatholigist at all. Dr. Jensen says that he believes that you can differentiate histologically whether the reaction might be due to hypersensitivity reaction or dietary, that you may be able to tell this on histopathology.

Question: Dr. Frey is behind the podium here so I'd like to ask him. Could you elaborate more on your gnotobiotic calves and your attempt to reproduce shipping fever by injecting the different known etiological agents, and what were some of your findings?

Answer: I could tell you briefly what I had on the few slides remaining which did deal with the combination infections. We didn't know quite where to begin on combination infections because there are endless