McChesney, A.E., Benitez, A., and Christie, R.M.: Shipping fever pneumonia in yearling feedlot cattle. JAVMA 169:500-506, 1976. 6. Johnson, D.W., Muscoplat, C.C., and McClure, J.J.: Immune responses to bovine viral diseases: BVD, IBR, and PI_3. Minn Vet 17:15-22, 1977. 7. Kahrs, R.F.: Rational basis for an immunization program against the common diseases of the bovine respiratory tract. Can Vet J 15:252-256, 1974. 8. Kahrs, R.F.: Infectious bovine rhinotracheitis: A review and update. JAVMA 171:1055-1064, 1977. 9. Lambert, G.: Bovine viral diarrhea: Prophylaxis and postvaccinal reactions. JAVMA 163:874-876, 1973. 10. Lillie, L.E.: The bovine respiratory disease complex: Can Vet J 15:233-242, 1974. 11. Mansfield, M.E., Crandell, R.A., and Woods, G.T.: The effect of intranasal IBR-PI_3 vaccination of feeder cattle on arrival at a feedlot compared with vaccination at the start of an outbreak of acute respiratory tract disease. Bov Pract 13:83-87, 1978. 12. Martin, S.W., Meek, A.H., Davis, D.G., Johnson, J.A., and Curtis, R.A.: Factors associated with morbidity and mortality in feedlot calves. The Bruce County Beef Project, Year Two. Can J Comp Med 45:103-112, 1981. 13. Muscoplat, C.C., Johnson, D.W., and Teuscher, E.: Surface immunoglobulin of circulating lymphocytes in chronic bovine viral diarrhea: Abnormalities in cell populations and cell function. Am J Vet Res 34:1101-1104, 1973. 14. Rosner, S.F.: Complications following vaccination of cattle against infectious bovine rhinotracheitis, bovine viral diarrhoea-mucosal disease and parainfluenza type 3. JAVMA 152:898-910, 1968. 15. Shaw, K.E. and Nichols, R.E.: Plasma 17-hydroxycorticosteroids in calves. The effects of shipping. Am J Vet Res 25:252-253, 1964. 16. Sheffy, B.E. and Williams, A.J.: Nutrition and the immune response. JAVMA 180:1073-1076, 1982. 17. Todd, J.D., Volenec, F.J. and Paton, I.M.: Interferon in nasal secretions and sera of calves after intranasal administration of avirulent infectious bovine rhinotracheitis virus: Association of interferon in nasal secretions with early resistance to challenge with virulent virus. Infect Immun 5:699-706, 1972. 18. Weiss, D.: Transport and respiratory disease among feedlot cattle related to changes in biochemical and cellular profiles. Master's Thesis, Kansas State University, Manhattan, KS, 1977.

Panel Discussion

Question: The question is in using Synovex-S on heifers.

Answer: I don't know exactly if there has been any real good research done on that or whether we're picking up just shop talk. I don't know, maybe Dallas would be able to answer that a little better than I do in the feedlot situation. We didn't see any problems with it on any of the trials that we have done.

Answer: I would just add to what you have said. Comments, shop-talk, without documentation. I don't know of a well-controlled, replicated study with good statistics that says there is a difference.

Question: Do you see more vaginal prolapses with either of the implants?

Answer: Here again, speaking of spayed heifers, we've seen no difference. As far as implants and prolapses in general, I think this again has a lot to do with the particular set of heifers, the particular environment and I don't know whether I could really say that Ralgro or Synovex can be incriminated as far as producing vaginal prolapses. I don't think we can. I think it backs up to that particular individual set of animals. It probably has more influence on it than our implanting. If I understand you right, what you interpreted off of our slides is that the cost of gain on an intact heifer was less than a spayed heifer. . . . this is referring to strictly intact heifers and the cost of gain between implanted and not implanted. I don't think there was a significant difference on it.

Question: Where did you start your base line to figure the cost of gain in spayed females?

Answer: That was started at the time of the feeding. These were all spayed during the grass feeding period so it was at entry into that feedlot. I think that probably the data didn't come out very well in favor of implanting intact heifers, but I don't think that I would stop with that all the time. I think I would have to agree that over the years the trials show there is an advantage to implanting intact heifers.

Question: The comment here is on theoretically spayed heifers coming into the feedlots and that is more like a tubular ligation. The question is, if there are ovaries in there, would you still have to drop down the inability to become pregnant, would you still have to consider this as an intact heifer?

Answer: Yes, because unless that ovary is atrophied, if it can still function and they are coming into heat, they are still getting the estrogen stimulation, the growth promoting stimulation from that ovary.

Question: What about interferon?

Answer: If interferon is present, it ought to help protect against BVD. Now if you look at Todd's work in 1972 when they first published the article about intranasal vaccines, and read the discussion part, they mention in there heterologous protection. They were able to demonstrate protection with IBR vaccination, interferon protection against BVD. He never discussed any more than that. He never published any more and I called him one time just to ask him just what was that data. What they saw was a one-day delay in fever to BVD because of the presence of interferon. And so, depending on the challenge dose, you can demonstrate good protection against the challenge. If you can overwhelm interferon . . . interferon is not just something that holds everything back . . .and we did some challenge work not with BVD but with PI_3, used IBR virus up the nose of calves, induced interferon came back with PI_3 as a challenge. We challenged calves with 10^5 units, 100,000 virus particles, and showed excellent protection in those calves. We had some other calves which we challenged with 10^8, which is a thousand times more virus and so no protection with the interferon. It overwhelmed the interferon response. And so depending on the challenge dose you ought to see good or bad results. If you have a little bit of BVD virus around it is susceptible to interferon and you will see some benefit from the interferon. If you have an overwhelming challenge, you won't see any benefit from the interferon.

If I put PI_3 up the nose of a calf, I get a little interferon. I don't know why I don't see more interferon in the nasal passage. — The best interferon inducer *in vivo* seems to be IBR. That's a DNA virus. That goes against what we think. The RNA viruses are supposed to be the best inducers, yet IBR vaccine does a much better job of producing interferon in the nose than any other vaccine. I even took the bluetongue virus and sprayed that up the nose of calves. That's a double-standard RNA virus. In the laboratory that is my best interferon inducer. But up the nose of a calf I hardly get any interferon at all. It has to be a replicating virus. It has to be something that grows and stimulates interferon production.

Question: What do you think the response of the pharmaceutical companies will be to the proposed changes in the Federal Register?

Answer: I've talked to two. One told me they were all set up to produce vaccine the way they produce it and they don't expect to change anything. Another one told me they expect to run their immunogenicity test over again and reduce the amount of virus in the vaccine. And so I think overall in the long run it probably will be cheaper for them to make. I think they'll probably charge us the same thing for a tenth of a dose. But those are proposed changes. They have to be addressed and discussed by December 27, and then some decision will be made by the USDA. We're not looking at antibiotics. Normally our studies are done without any antibiotic. They are on feeds without rumensin or any feed additives and so basically we're trying to locate interferon. When we start to get real high death losses we start to use some antibiotics. It doesn't really seem to help us any, but we have used some antibiotics. The area that interests me the most for antibiotics and vaccine are the bacterins. We're going to start seeing on the market live pasteurella vaccine. The killed pasteurella products don't work very well. They work great in mice. They're tested in mice and if we ever grow mice in the feedlot we'll have an excellent vaccine for them! But we don't have the super pasteurella vaccines that we need in cattle. They seem to be coming in the form of live pasteurella vaccines. Those seem to be protecting and I think we'll see those, but they are susceptible to antibiotics. And so how are we going to use antibiotics and vaccinate with a live pasteurella product when we'll neutralize our vaccine? That will be the question, when do vaccines and antibiotics really interact? It will be in our bacterins, I think.

Question: You vaccinate a hundred pound calf and a thousand pound with the same dose of vaccine. Shouldn't there be some gradient in the dose?

Answer: If you put the intranasal vaccine up the nose you're not putting all the vaccine virus there. You're putting a little bit that grows. The injectable is a different thing. That's what you put at the sight. The immunogenicity test is done on certain sized animals. Maybe there is a difference. I think that, frankly, nobody knows your answer, but I don't think it makes a lot of difference. There is so much excess for all sizes. Maybe if we start diluting vaccine it will get to the point that we will need more antigen in some of the different sizes. One of my contentions is that you will see better performance by giving less vaccine virus. More is not better when it comes to vaccine virus. I think you'll actually see better performance with a tenth of a dose than you will see with a full dose, simply because I did the other. I used ten times doses. I put ten times doses up the nose of calves and I used a product which is an excellent one, but I used it in 9 calves and all 9 of them developed IBR. I created the disease with excessive amounts of virus. You create an infection. The immune response is somehow related to how many cells you infect in the beginning. If you throw a lot of virus in there and infect a lot of cells, you get a lot of immune response. You get a lot of cells responding in the immune response. But if you infect a few, then you just generate fewer cells into the immune response and it takes less energy.

Question: In a feedlot in which you vaccinate upon arrival and then 21 days later, are you using the same kind of vaccine each time, intranasally or intramuscularly?

Answer: I have used intranasal for revaccination to see if I could restimulate interferon. I did it, not within 21 days, but within 56 days . . . I've forgotten the exact time. I could not demonstrate any interferon. I did not have enough antibody or protection where I just blocked my vaccination. In many cases, if you are getting a very good response to your first vaccine, you ought to really block your second vaccine for the most part. Now if you are not getting a good response the first time, then coming back and revaccinating you ought to pick those calves up. You ought to be getting some benefit in those calves. Are the breaks as you see it at 56 days really IBR breaks? Or are they something else? We go to the diagnostic laboratory with one of these calves that dies at 56 days, and they always find IBR virus. We put live vaccine virus in them. And so they'll swab that calf or isolate IBR from the tissue. What does that mean? Does that mean there's an IBR break? Probably vaccine virus that the diagnostic laboratory reports back to us.

Question: Were the breaks he was seeing related to IBR?

Answer: I think you basically answered the question beforehand. We had IBR in there and in revaccination we put more IBR in there and we had a difficulty finding out if we had that as an original problem. So I can't tell you if we saw it or not. When you talk about revaccination at 21 days that bothers me. We should have an antibiotic titer rise by that point in time. You go back and look at the work, you'll see that by 7 days we start getting a titer rise. It is our contention that if we reprocess it prior to that rise then we should get that one or a larger population, the ones that didn't respond the first time. This was priliminary data that was run. There were about 3,000 head that we showed you the results on. I think there needs to be some further work done on it, looking at titeral activity, looking at interferon activity, looking at viral titers on these things before we can give a definitive answer on it, on why potentially it works that way.

Question: When the calves are reprocessed, do they get antibiotics?

Answer: Yes. We were actually pulling calves out of these pens that were doing well and the calves going in the treatment pen were vaccinated just the same as those that were going back into the home pen. So we were vaccinating sick animals and I think, from the one piece of data that we showed, the relapse rate on the ones put back in, were decreased. How and why they respond I really can't tell you. I am concerned that if we have an antibiotic and it doesn't have the protein synthesis that we might interfere with active immunization procedures. An antibiotic that comes to mind is oxytetracycline. It does interfere with protein synthesis. If we use this particular product, will it interfere with antibody response? I know there are millions of injections made with

it and we've seen people benefit from it, but what is it doing? We're trying to run a research trial on that, just about concluded now, to see if there is an interference with it on our responses on single vaccination.

Question: What is the advantage or disadvantage of using intranasal vaccine on young calves in a cow-calf operation, instead of using intramuscular vaccination at that time?

Answer: If I am vaccinating a calf that has colostral antibody and if I use an intramuscular product in the face of large colostral antibody, it is conceivable that I could block my vaccination. But colostral antibody doesn't live in the nose. And so if I use an intranasal vaccine I still ought to get some local replication and perhaps some protection from the intranasal product in the face of the colostral antibody, theoretically.

Question: What about the duration of antibody response to intranasal versus intramuscular?

Answer: We generally run studies for 56 days and we get rid of the calves because we've got all the capital tied up in these calves and so at the end of 56 days we sell them, buy new calves and start another study. So I don't have a whole lot of duration information for you. But I can tell you at the end of 21 days or 28 days or anytime that we look, we do have, or seems to be, higher antibody titers with the intramuscular products than we do with the intranasal product. That doesn't mean it won't last for ten years, but they are higher with the intramuscular product. It seems to be a stronger antigen, even though the other is replicating in the nasal passage.

Question: What about the duration of ant body response the nose?

Answer: Not that we can see. It replicates locally at the muscle, sight of the injection, and that's it. And so it stimulates there.