General Session

Dr. Robert Harris, Chairman

Nutrition and Its Subsequent Effects on Diseases

Ben Norman, *D.V.M., Ph.D.*
Extension Service
University of California
Davis, California

I would like to talk to you today about the interaction between disease and nutrition. So that we all have the same basis of discussion–semantics is one of the problems that occurs between veterinarians and consulting nutritionists–let's talk a little bit about synergism, antagonism, primary and secondary malnutrition. The simplest definition of malnutrition is too much or too little of a required nutrient. By that definition I am malnourished by about 40 pounds.

Synergism is where the simultaneous malnutrition and the disease cause a more severe animal response than either one of them alone. Antagonism is where the malnutrition produces the severity of concurrent disease. We will show you some examples. Now, part of our problem is the consulting nutritionist is trained in primary malnutrition or primary nutrition and the things we see deal with primary malnutrition and secondary malnutrition. Definition of secondary malnutrition would be too much of a nutrient, not enough of a nutrient, or an improper balance of some nutrients. You and I have to go beyond that. We also deal with animals in the stage of secondary malnutrition. Animals that have increased needs due to fever, animals that have decreased absorption of a good ration, perhaps due to diarrhea. Then there are animals that have a metabolic disorder that cannot utilize certain parts of the rations, diabetes would be an example. Animals that have an immunologic disorder. There are a number of situations in the dog that are described. For example, the dog is immunologically antagonistic to wheat proteins, to glutin proteins, and it causes problems. Sure, this exists, but it is not documented in large animals.

Now, at Davis we like to duck-hunt a lot and I took a statistician out duck-hunting with me one day and he took a double barrel shotgun. A goose flew over and he fired once and he fired ahead of the duck or the goose. He fired again and he missed and he fired behind and he turned to me with a puzzled look on his face and said, "On the average, he ought to be dead." That is the problem that you and I deal with. You and I deal with the animals that fall between the cracks as well as those that are on the average. Those animals that fly between the patterns.

Here is an example of dogs, standard beagle dogs, under weight-maintaining situations, maintaining their weight under laboratory conditions, and we are talking about animals that vary from 23 to 39 pounds. Let's look at it the way you and I count our situation, here. Let's look at these animals–the pounds of feed that are required of these animals per pound of dog. Here is 0.03 pounds of feed, a 0.4, a 0.5, a 0.47, a tremendous percentage difference in the amount of feed required for these animals. But look out here at the difference in the kinds of animals, yet, that would not show up in a standard nutritional table. These animals would be fed, quote, "on the average." Here we know that different animals under different conditions have different requirements to maintain weight, just for example.

Similar work with cattle at Cornell showed that when you fed hay in the morning and silage in the afternoon that the animals ate on an average a given amount, but when you looked within the groups, some animals made almost 20% of their ration out of hay. Some ate almost 80% of their ration from silage and there was the inverse group. Some of them ate almost 20% of their ration from silage and 80% from hay. Yet, we looked at the herd on the average. The other problem we have in dealing with disease in nutrition is that people that we deal with judge things the way they are trained, not the way we are trained. An example here is an experiment that was conducted where the shaved tummies of a group of sheep on a high plane of nutrition and a low plane of nutrition were injected with cultures of *Staph. aureus* under the skin. Twenty-four hours later the animals were looked at and these were the responses. On the animals on the good plane of nutrition, there was a large area of inflammation on the skin. On the animals with the low plane of nutrition, the skin there showed no sign of inflammation, just a small mark

where the needle went in. The nutritionist not being trained in pathology would have looked at that and said, "Gee, look, low plane of nutrition gives protection." The veterinarian would have looked at it and said, "Gee, the low plane of nutrition destroys the ability of the animal to resist." Sure enough, when they cut in there and took sections out and looked at them under the microscope, they found that in the high-inflammation area they could find very few bacteria in the subcutaneous tissue and in the low-inflammation area they found many bacteria colonizing the subcutaneous tissue. So we have a difference here as to how a nutritionist untrained in pathology might consider a response differently from what you and I might consider, and we generally have the histologic tools and they do not.

In general, with bacterial diseases, the well-nourished animal has a lowered incidence and a reduced severity in malnourished states, as a general statement. Well, you say that is fine. In parasitic infection, well-nourished animals have higher resistance and recover faster than malnourished animals. But let's look at the case of the viral infections. Now, we are talking about viral infections that are perhaps uncomplicated by secondary bacterial invaders, but in viral infections, well-nourished animals tend to be more susceptible to diseases of viral nature. Think about it. The virus has to take over a cell to reproduce itself. If the cell works better because it is well nourished, perhaps it is a little easier to move in there and reproduce itself.

I think the exception that we need to remember is that when a specific nutrient deficiency reduces the parasite's or the intercellular parasite's ability to reproduce, then we can see an antagonistic situation where a deficiency state may inhibit the development of these.

A more simple way of remembering synergism and antagonism is that synergism is the usual result from the major impact of malnutrition on the animal and antagonism is the usual result when the major impact of malnutrition is on the disease agent.

Now, I would give you an example of antagonism. The case of the single calf with anaplasmosis maintained on a very low magnesium diet. Data from Miller and Bedell. If we infected the animal at day zero we would expect a parasitemia of 35 to 40% in that calf. I have infected a large number of calves. What happens on the average is that at 28 days they get 1% of their red blood cells parasitized. In this case, out to fifty days there was no visual, clinical or parasitological effect on the red blood cells in a calf with a very low magnesium diet.

Diet change. The animal is put on magnesium-sufficient diet. What happens? About fifteen days later, the animal starts to develop a parasitemia and in about 80 days the animal dies. A situation here where anaplasmosis has been suppressed by a specific nutrient deficiency and has been released when the animal has been re-fed.

The literature is very scarce, particularly when you talk about large animals that you and I deal with. There is a study done by the World Health Organization which is probably the master study on the interaction between disease and nutrition and it was published in 1966. Over the world literature, they count less than 500 reports that they considered of scientific merit with good controls as far as actually studying the interactions between disease and nutrition, all species, all nutrients.

We look at these reports divided up on the basis of bacterial and rickettsial disease, viral disease, protozoal diseases, and we obviously have come up with the same data divided a different way and we find 15%. But we look at the data internally and we see that of the bacteria and rickettsia, only 6% of them showed any antagonism. We look at the viral diseases and we show that 35% of the malnourished animals exhibited less disease response to the virus than those animals that were not malnourished. We come to protozoa and we see basically the same thing. We come down to helminths and come back to our average of about 15%. I would look at it the other way. Fifteen percent from 100 is 85%. Eighty-five percent of all of the diseases studied in this group or reported in this group of studies were influenced either favorably or poorly by the state of nutrition of the animal.

In only 15% of the cases did nutrition have a bearing on what happened to the animal when it developed disease. When I was going through school, we treated retained placentas with a little bit of antibiotic and turned them out. This is an example of some farm work done in Ohio where herds with injected animals had less retained placenta than herds without injected selenium. Of the animals that were on a deficient ration that were not injected with selenium, depending on the other nutrient levels, between 20 and 50% came up with retained placenta.

What does it do to nutrition? Very few controlled studies show the changes in digestabilities due to malnourishment. Now here is a situation where the parasites were changed in graded loads, so that we have animals in the control groups that were not given any parasitic larvae and we have animals that are in the other groups that were given up to 8,000 larvae. We are talking about sheep. When we got through looking at the voluntary consumption, the control animals were eating on an ad-lib basis about 20% more than the highly-infected animals on an ad-lib basis. When we looked at the apparent dry matter digestability and apparent food protein digestability, add those together, the heavily infected lambs utilized about 10% less of the nutrients that they did consume than those that were not infected.

The by-products of bacteria can also cause diseases, as we know. Here is an example of pigs and the endotoxins of *E. coli.* Surviving endotoxin challenge at 28 days versus iron supplementation. Iron-injected pigs, 100% survived the challenge at 28 days. When pigs without iron were injected, only 1 in 4 survived the endotoxin challenge, so it does not have to be live

bacteria. It can also be the by-products of those organisms.

Here is an example of the influence of "good nutrition" or high levels of nutrition on viral diseases. Canine distemper and ration energy. A low energy ration, a normal energy ration, and a high energy ration. Dogs fed under experimental conditions for six weeks until they maintained a given consumption per day, and then exposed to street virus or a standard dose of distemper virus. What happens? Survival time on the low plane was higher by almost 50% than those animals on the high-energy diet.

We look at the incidence of paralytic encephalitis and we see that in the animals on the low plane of nutrition, only 1/3 of them had paralytic encephalitis. It goes all the way up to 90% on the high-energy plane. How come before we started feeding 55% concentrate rations in feedlots, we seldom had problems with IBR. One wonders about the relationship. This leads into some situations in cattle, I am sure. What happened here, we have a group of bitches that were fed only 1/3 of their protein requirement during gestation. We have the same type of bitch being fed 100% of her gestation requirement for protein. As soon as they were whelped, they were fed 100% of their lactation requirements in protein for lactation. We look at the puppies from those bitches and at six months of age they cannot be distinguished clinically. Their weights overlap around 20 pounds. The pups are challenged with distemper virus and of those of the deficient mother, 26 of 35 developed paralytic encephalitis. Seventy-five percent developed paralytic encephalitis.

Of those whose mothers were fed sufficient ration, only 12 of 35 pups developed paralytic encephalitis. One third of them developed the disease. How many times do we see animals that we treat that respond or do not respond due to a situation like this over which we have no control? A biochemical lesion that has persisted since intrauterine assault as far as nutrition is concerned.

Those of you that attended the theriogenology meeting heard Dr. Dunn talk about a group of calves. This is part of the situation, low cows and high cows, meaning cows during the last 100 days were fed a maintenance diet. They were not well fed. We look here and we see they were fed 8.4 megacals, but in one group half of those animals were supplemented with an adequate energy level during the last 30 days before calving. And then as soon as they lactated they were all fed the same ration. Now 28.8 megacals or just some energy supplementation, thirty days before, and what happened?

They had the same number of calves born. But, in that pen, the cows were all running together, they developed a case of scours that went through the whole group. Fifty percent of one of the groups developed scours and 35% of the other group developed scours of these two sets of calves. So, no statistical difference in that number, but there was a difference. When the veterinarian was called out to treat, those that came from the normal mother responded to the medication and lived. They wound up with 19% pure calves from the mother which had cheated on energy during her gestation period, yet there was no difference in the scours situation. We see this we think in California with selenium-deficient animals. They just do not respond to treatment until you apply some injectable selenium. Then the antibiotics start to work. Then your management practices start to work.

I would like to close with something that is related to cancer and malnourishment. Here is a group of animals, Hereford cattle with cancer eye. A group of animals that were fed in Oklahoma from the time they were first-calf heifers until they died of old age on a range near Oklahoma City. They were supplemented from November to April. The rest of the time they were on pasture. Supplementation for group one or the low group was just one pound of cotton seal meal per head per day. This is the incidence of the number of sites in the eye with cancer, cancer eye, from 6 to 9 years of age. Now that was thought to be a very low supplementation plane at that time and this was supposed to be the control group. These animals had two and a half pounds of cotton seed oil meal during the winter period on dry native range during that period of time.

And here is a significant difference and response. The development of squamous cell carcinoma in these animals. And here is the high group. These are animals that were fed cotton seed oil meal plus three pounds of oats. You can see a direct response here to the levels of energy, the levels of supplementation and the development of these lesions around the eyes of the animals.

I really would like for you to go back to your practice and think about the interaction between malnutrition and disease and remember that in 85% of the cases nutrition will influence the outcome of the disease entity that you work with.