ALPACA RESEARCH FOUNDATION

Dealing with Barber's Pole Worm:

ARF Funds Study to Test Safety and Efficacy of Barbervax Vaccine

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In the Autumn 2016 issue of *Alpacas Magazine,* Dr. Williamson from the University of Georgia College of Veterinary Medicine, provided an introduction to *Haemonchus contortus,* the Barber's pole worm. She highlighted some potential control measures, the importance of farm biosecurity, the significant loss of dewormer efficacy as worm populations rapidly develop drug resistance, and the utility of the FAMACHA System for selective deworming. These are standard armaments producers can use in their battle against the Barber's pole worm. Recently, the sheep and goat producers in the world down under (Australia) gained a new tool to use against Barber's pole in their flocks. Barbervax is an approved vaccine in Australia for use in sheep.

Barbervax is a result of more than 20 years in research and development by the Moredun Research Institute in Scotland. Dr. David Smith was instrumental in understanding the biology of the parasite, targeting the relevant worm gut proteins ("hidden" antigens) to use in the vaccine and evaluating the vaccine in Australian field trials.

This vaccine is uniquely designed to target hidden parasite antigens. The vaccine antigen is the H-gal-GP, a worm gut membrane associated multiprotease complex, which is involved in the digestion of the blood meal taken up by the *H. contortus* worms. The H-gal-GP protein complex is mixed with an adjuvant (a substance that enhances the body's immune response to an antigen) to cause vaccinated animals to develop antibodies to this H-gal-GP protein complex. Antibodies ingested by the worm then bind to the complex inside the worm's gut, causing the parasite to starve and eventually die.

The major benefit of this scientific discovery is the adult worms (blood feeders) cannot digest blood and cannot produce eggs when starved. This apparently occurs to both drug sensitive and resistant worms. The inability to take the required blood meal ultimately leads to lower parasite numbers in animals, lower shedding of parasite eggs into the environment, and improved health for sheep and goats with less frequent treatments for parasite-associated anemia.

In large field trials of vaccinated sheep (including young lambs, pregnant ewes and second-grazing-season sheep) parasite egg shedding, measurements of antibody titers to the H-gal-GP protein and overall health scores were analyzed. Generally, the vaccinated animals showed significant differences in these parameters measured, as compared to unvaccinated animals. There were no adverse events when the vaccine was used in pregnant ewes. Meat and Livestock Australia, in conjunction with the Moredun Research Institute, published a number of these sheep field trials to register Barbervax for use in lambs, yearlings and ewes. It is now sold commercially in Australia.

The number of goats in Australia is less than the sheep population. However goats, as well as alpacas, llamas, camels

Michelle Carman (left) and Dr. VanHoy (right) stand with one of the alpacas that will participate in the first safety trial of the vaccine.

Photo courtesy of the authors

and other ruminants, are susceptible to the Barber's pole worm. Additional vaccine label approvals within a country for a specific animal species and age requires significant financial and resource outlays by the sponsors of the research, which may include the vaccine production company, industry stockholders, and research and development groups. The number of animals, the market share, and governmental licensing requirements will determine whether a vaccine study is pursued for later commercial development and labeling. At this point, Barbervax is only labeled for sheep and is not labeled for goats or other ruminants. Moreover, it is not approved for use in sheep in the United States, despite all the work done in Australia.

Ohio State University is interested in understanding the immune responses of alpacas, including how they would respond to vaccination with Barbervax containing the H-gal-GP protein complex and adjuvant. Camelids produce conventional antibodies similar to sheep and goats, and also produce a unique type of antibody which is devoid of light chains (part of the overall antibody protein). These light-chain-devoid antibodies are called heavy-chain antibodies (HCAb), and are structurally smaller than conventional antibodies found in sheep, cattle and even humans.

A company, Ablynx, is focusing on the non-veterinary therapeutic applications of camelid antibodies because of their small size, biological activity and ability to get into small spaces. Research by Padula et al, published in *Toxicon* in 2016, demonstrates that alpaca antibodies from hyper-immunized alpacas will neutralize toxic venom enzymes. Thus, the small size and conformational structure of alpaca HCAb specifically targeting the H-gal-GP multiprotease protein of *H. contortus* may bind and inhibit this worm enzyme complex even better than the conventional antibodies generated in vaccinated sheep or goats.

As a first step, it is important to determine if the vaccine antigen will be safe when administered to alpacas. Although many vaccines are used in camelids, most have never been scientifically evaluated or approved by regulatory agencies. After several thousand doses of *Clostridium perfringens* types C, D and tetanus bacterin/toxoid have been used in alpacas, one can say camelids may have reactions. However, the observed reactions are not much different than in the species they are approved for. The Barbervax vaccine should be tested in enough alpacas to be able to corroborate this.

Also, it has been observed that camelids mount immune responses to vaccines approved for other species. Vaccines against West Nile virus, Eastern Equine Encephalitis virus, and even Rabies generate immune responses in camelids immunized with these vaccines. In addition, while not objectively evaluated yet, the special properties of HCAb camelids produce should be beneficial to camelids as well. The Barbervax vaccine will likely result in production of antibodies to this worm protein.

As a second step, it is important to generate evidence the vaccine is not only safe and immunogenic, but also effective. For any intervention, carefully designed and controlled experimental trials are necessary to isolate and precisely measure the effect of a treatment or prevention practice.

In this case, our objective is to measure the reduction in fecal egg counts attributable to vaccine administration. To do this, a control group must be selected that is similar in all respects to the vaccine group, with the exception of the vaccine exposure. Precise and well-timed measurements of fecal egg counts will be used to measure changes over time. To prevent unintentional biases, investigators measuring this outcome will be blinded

to the group assignment of the animals enrolled in the study. A sufficient number of animals and measurements are used to ensure that any measurable and biologically important differences between the vaccine and control group are unlikely to occur due to natural or random variation in fecal egg counts. Lastly, robust data analysis procedures are necessary to determine if the temporal changes in fecal egg counts in the vaccine and control group are statistically significant.

Through the approval of the Animal and Plant Health Inspection and Veterinary Services along with the State Veterinarian of Ohio, Ohio Department of Agriculture, Ohio State University's College of Veterinary Medicine received approval to import Barbervax for use in an alpaca safety and efficacy trial. Dr. David Smith is supplying the vaccine. Our research team is composed of a parasitologist (Marsh), veterinary internal medicine specialist (Lakritz), and epidemiologist (Habing), along with a large animal internal medicine resident, Dr. Grace VanHoy and her assistant, veterinary student, Michelle Carman. Dr. Ray Kaplan, University of Georgia, whose expertise includes ruminant nematodes, will also collaborate on the project.

We look forward to sharing our finding in the near future about using the vaccine to immunize alpacas. We expect this collaborative effort to yield important results for alpaca owners. But until we know more, keep scooping the dung pile to limit your friends' exposure to the Barber's pole worm.

The authors and trainees thank the Alpaca Research Foundation and their donors for supporting this trial. ■

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