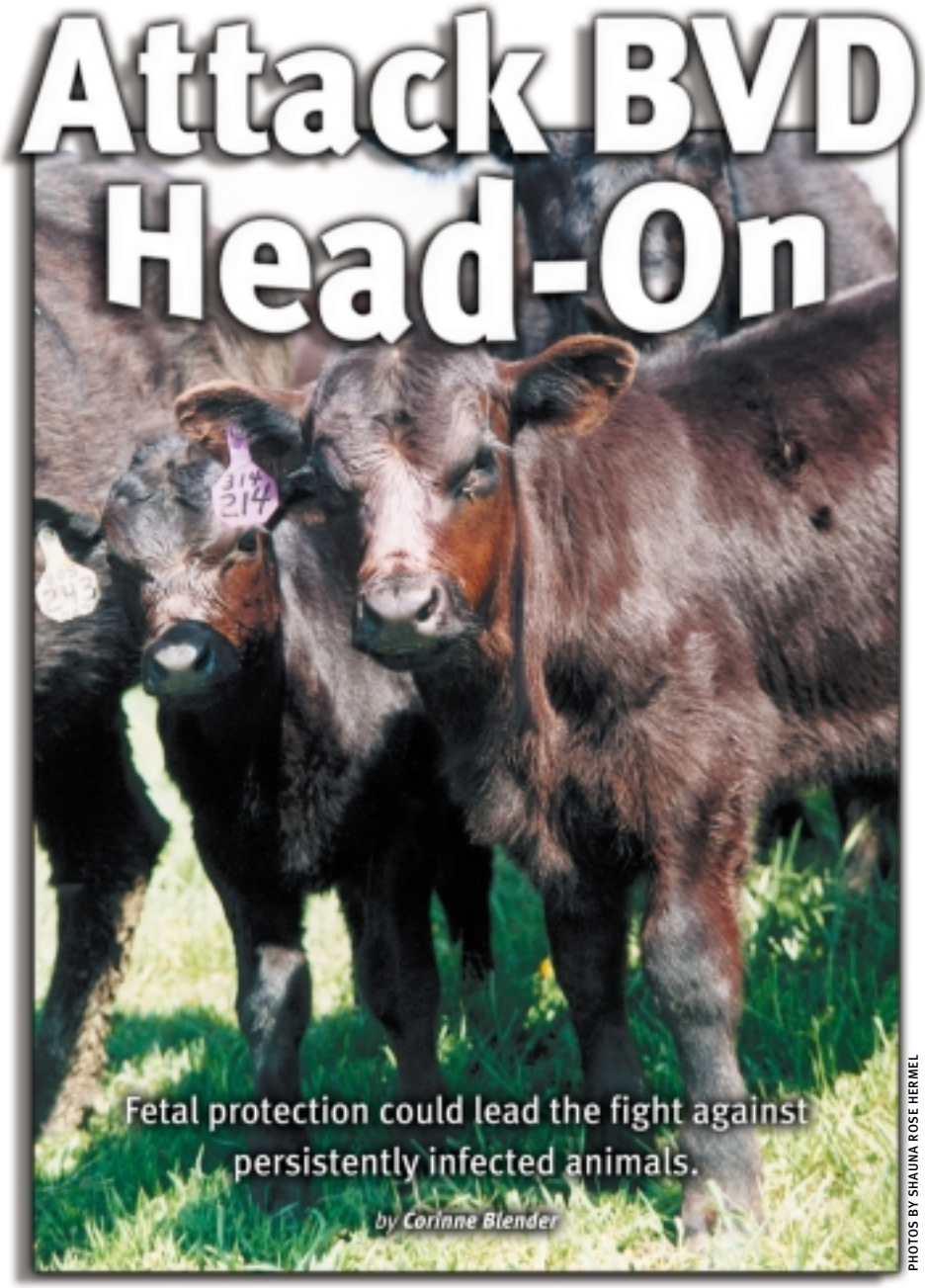
Attack BVD Head-On



Fetal protection could lead the fight against persistently infected animals.

by Corinne Blender

PHOTOS BY SHAUNA ROSE HERMEL

Protecting the fetus from infection is the newest, and perhaps most effective, means of battling bovine viral diarrhea (BVD).

Fetal infection during the first 50 to 120 days of gestation can lead to the birth of persistently infected (PI) calves, the major contributors to the spread of BVD, says Carol Rinehart, manager of bovine biological research and development at Boehringer Ingelheim Vetmedica Inc. (BI).

Animal health companies, including BI, a Saint Joseph, Mo., based company, are focusing on products that will provide fetal protection to prevent the birth of PI calves. BI received approval for its Breedback™ FP 10 vaccine with a new fetal protection claim in October. Other products approved for fetal protection include Bovi-Shield™ FP and PregGuard™ FP, by Pfizer Animal Health; and Jencine®4, by Schering-Plough Animal Health.

"PI calves are born tolerant to BVD, which means they do not recognize that the virus is different from self," Rinehart explains. "They are not able to mount an immune response against the virus, and they are capable of shedding enormous amounts of the virus into the environment," she adds, which puts the rest of the herd at risk. Those PI calves are "the gift that keeps on giving."

PI calves are not the only concern BVD infections during pregnancy cause. "Depending on what part of gestation the animals [become] infected in, BVD can cause abortions, mummification of the fetus and, of course, more persistently infected calves," Rinehart says.

Best defense

Researchers say cattlemen can begin the first step to mounting an attack against BVD in their herds by providing protection during pregnancy. "The emphasis is to try not only to get the PI calf out of the herd, but also to use a vaccine that is capable of protecting a fetus against BVD virus," says Phil Widel, senior technical service manager at BI.

Rinehart recommends vaccinating cows four to eight weeks prior to insemination, with a vaccine that has a fetal protection claim. BI's vaccine is a single-dose, modified-live-virus (MLV) product.

"It should drastically cut down on the number of BVD infections," she says. "It should prevent the birth of persistently infected calves, which will reduce the exposure to both type 1 and type 2 BVD."

Many cow-calf producers are concerned about using MLV vaccines because they can cause a cow to abort if not used according to label directions. But Rinehart says that MLV vaccines, when used properly, may be the only source that provides fetal protection.

"If a producer is concerned about the use of a modified-live product, then there are some decent inactivated BVD vaccines on the market," Rinehart says. "But they have to be used correctly, and they have to be used prior to insemination so that the level of immunity in the cow or heifer is at the point where it will give the best chance that the fetus will be protected. If the vaccine is a two-dose vaccine, both doses must be given prior to insemination, using the recommended dosage intervals.

"I do not believe that there are any *inactivated* vaccines that currently have a fetal protection claim on the U.S. market," she says. "The only ones that have a fetal protection claim are modified-lives. It is very hard to induce the level of immunity required to protect the fetus with an inactivated vaccine."

Learning more

The knowledge gained about BVD in the last few years has really advanced the attack against its spread in beef herds.

In the early 1990s, researchers discovered a second genotype (type 2) when an outbreak of BVD hit the Northeast, Widel says. Herds were being vaccinated with a killed product, but were not always being given the booster shot required when using killed vaccines.

"It is not always handy to bring cattle back into the corral and run them through and give them their booster dose," Widel says. In many instances, he adds, the producer may either not give the booster at all or may opt

►**Above:** In an effort to control BVD, animal health companies are focusing on vaccines that protect the fetus, thereby preventing the birth of persistently infected calves, which can shed enormous amounts of the virus into the environment and put the rest of the herd at risk.

to wait three or four months until they are working the cattle for another reason. "They give the booster then, thinking that it is still a booster. In reality it is not. By then, the system that's been primed with the first dose has lost its level of immunity."

Whether the vaccine is inactivated or MLV, Rinehart says it is important to include protection from both type 1 and type 2 BVD. "The synergy between those two strains in the vaccine will give you higher titers and a broader coverage than a single-isolate vaccine," she adds.

Widel says that just because the cow is protected doesn't mean the calf will be protected. "The cow's immunity is only going to be passed to the calf after it is born, through the colostrum milk," he says. "The cow is not like the human where they can actually give antibody from their own blood to the fetus. The bovine fetus is very vulnerable, and if the virus is able to cross the placenta and get into the fetus at a certain stage of pregnancy, then it produces persistent infection."

The mother cow's protection is important as well, but fetal protection isn't guaranteed just because the cow is vaccinated. The vaccine must produce immunity strong enough to prevent infection of the fetus.

"We do know that there is a high correlation with protection of the fetus with a high antibody titer in the dam," Rinehart says. "Researchers are spending more time evaluating cell-mediated immunity and its possible role in protection of the cow and fetus. The next five years will tell us a lot more than what we know now on exactly how the fetal infection happens with BVD and what mechanisms are important in protection of the fetus."

Stop the cycle

If there are some indications of BVD in a herd, one should test the herd to find any PI animals and have them removed. But remember, the fact that a herd has been tested free or has culled any BVD PI cattle doesn't mean it will be protected, Widel says. He offers that the best things producers can do to protect their herds are to have a functional biosecurity plan in place that includes quarantining new animals, and to have a proper vaccination protocol.

"If producers do not watch their biosecurity, as far as keeping BVD out, then they are kind of spinning their wheels," Widel says. "They really need to have a biosecurity program, as well as monitor their herds occasionally to make sure they are not bringing something in. That's where most people get in trouble."

► If there are indications of BVD infection in a herd, Phil Widel recommends testing the herd to reveal any PI animals so they can be removed from the herd, then instituting a functional biosecurity plan in addition to a vaccination program.

When new animals are introduced, producers now have the option of having a skin test performed to see if the new purchase is a PI animal. Diagnostic labs across the Midwest use ear-notch samples because PI animals will have BVD virus in their skin.

Identify thy BVD enemy

"Persistently infected animals are usually the major source of BVD infection within a herd because those animals are born with the virus and shed the virus for their entire lifetime," says Bruce Brodersen, diagnostic pathologist and assistant professor of veterinary and biomedical sciences at the University of Nebraska-Lincoln (UNL).

Brodersen adapted a skin test to detect these PI calves. The test, performed at the University of Nebraska's diagnostic laboratory, is much simpler than blood tests, which previously were the only option for cattlemen.

"Persistently infected animals' immune systems do not recognize the virus, and so the virus is present in virtually all the cell types in the body, all tissues in the body," he says. "The skin sample is an easy sample to collect, and the test is quite reliable."

The test identifies PI animals because the virus is disseminated throughout their bodies. It rarely detects acute infections (cases that come and go). It is easy to collect a sample for evaluation, and it is inexpensive (about $3) to boot.

"The skin sample is fixed in formaldehyde before being sent to the lab, so there is no worry about keeping the sample chilled or anything like that," Brodersen says. "As opposed to collecting a blood sample that was necessary for previous tests, you don't have to try to hit a vein to get a sample, so it's easy to collect, and it's stable." The test usually takes four to seven business days to return results.

Last year, Brodersen says the laboratory received 100,000 BVD test samples. Approximately half were from beef cattle. Their busiest time is in the spring when producers are testing their calf crops. He

CONTINUED ON PAGE 134

Can you rely on cross protection for type 1 and type 2 BVD?

In the early 1990s several herds experienced outbreaks of severe bovine viral diarrhea (BVD) in spite of vaccination. Researchers began to look at the BVD viruses that were showing up in those herds and found a different BVD strain, type 2, using DNA fingerprinting, says Phil Widel, senior technical service manager at Boehringer Ingelheim Vetmedica Inc. (BI). "It had a considerably different code protein than type 1 BVD."

Some animal health companies began putting both type 1 and type 2 strains in their vaccines, but not all. "Some companies still are using a type 1 only and relying on cross protection," Widel says. "The virus does have some common base protein; approximately 60% of the virus protein is the same between the type 1 and type 2. That leaves about 40% that is different.

"There is a certain amount of cross protection based on that 60% that's common, but we feel, as well as some other companies that have put type 2 in their vaccines, that the vaccine virus proteins should match as closely as possible to what might be out in the field and is going to be challenging their herds. We have also seen that there is a synergy between the two vaccine components that provides enhanced immunity to BVD."

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CONTINUED FROM PAGE 133

cautions that producers shouldn't necessarily run out and test their entire herds unless they know they are experiencing a BVD problem.

"Certainly, they should test newly purchased animals, particularly replacement heifers and bulls," he says. "If someone purchases bred cows or bred heifers, the calves from those animals should also be tested because even though the dam may be negative, she could still have a persistently infected calf."

Tests should be followed up by a surveillance program of some sort, he says.

"Purebred producers, in particular, can use this as a marketing tool similar to herds that are screening for Johne's and other diseases," Brodersen says. AJ

Which calves are immune?

Research has shown that when calves nurse their mother's colostrum, they will receive antibodies to diseases such as bovine viral diarrhea (BVD) if their mother carries the antibody, says Jim Roth, an immunobiologist at the College of Veterinary Medicine at Iowa State University (ISU).

When the calf receives the antibody, it is protected for several weeks or months. But, Roth says, over time the antibody will decrease, leaving the calf susceptible to BVD.

"It is good that they get this antibody from the cow's colostrum. It protects them while they are little. But we would like to be able to vaccinate them so that they develop their own protection before they lose the protection they received from their mothers," Roth adds. "With essentially all vaccines, a problem in vaccinating young animals is that the antibody they get from the mother blocks the vaccine from working. It protects from disease, but it also prevents the vaccine from inducing antibody-based immunity."

To help understand the window of time when this occurs and to possibly eliminate it, Roth is measuring cell-mediated immunity in the blood of the calf. Cell-mediated immunity is an important type of immunity that is not due to antibodies.

"We've shown that you can take calves with maternal antibody, challenge them with virulent BVD when they are 1 month old, and they are totally protected. They don't get sick because the maternal antibody protects them, as you would expect," he says. "The novel aspect of our study was that we then waited until these same calves were 8 or 9 months old and had no antibody left, then we challenged them again and they were totally protected even though they had no antibody.

"During that time we were measuring T-cell reactivity to BVD virus. We were able to show that the first exposure induced cell-mediated immunity and memory B lymphocytes. These were responsible for protecting the calves even though they did not have any antibody. So the newer technology in immunology, the ability to measure T-cells and not just depend on measurement of antibody, helps us to have a much clearer picture of which calves might be immune and which ones aren't."

This new tool of immunology will likely be used by vaccine developers to measure T- and B-cell activity to more clearly determine whether the vaccine might protect the animal by inducing T and B memory cells and not just evaluate vaccines by measuring antibody. "Clearly, antibody isn't the whole story," Roth says.