Barberpole Worms—Parasites of Another Stripe

The barberpole worm is among the world's most loathsome and widespread stomach parasites of sheep, goats, and cattle. They feed on host animals' blood with a voracious appetite.

For farmers, the headache begins when approved drugs fail to protect their animals from this parasitic nematode that is better known by its scientific name, *Haemonchus contortus*. There seems to be evidence that the pest is showing signs of resisting the effects of such pharmaceutical controls. But new research under way in Beltsville, Maryland, could undermine the parasite's costly mischief by means of biochemical sabotage.

Agricultural Research Service zoologist Raymond H. Fetterer is leading the effort, along with chemist Marcia L. Rhoads, parasitologist Dolores E. Hill, and technician Ruth Barfield. Their chief focus is to identify and exploit natural substances that the barberpole worm secretes while using its host as both room and board.

By taking this route, they hope to set the stage for developing new drugs or, preferably, natural control agents "relatively specific to the nematode and nontoxic to the host," says Fetterer, who is at ARS' Parasite Biology and Epidemiology Laboratory in Beltsville.

The team's work comes at a time of growing concern over evidence that many nematode parasites may be developing drug resistance.

"In many parts of the world, including the United States, drug resistance is becoming a problem, particularly with *Haemonchus* in sheep," says Fetterer.

Going for the Gut

Scrutinizing the barberpole worm's biochemistry could yield much-needed alternatives, including new substances for creating animal vaccines. "We have a long way to go before that point," cautions Fetterer, "but we have some good candidates."

These include a potent cocktail of digestive proteins and enzymes the scientists recently discovered after cutting into the parasite's long, thin intestine. Their focus now: confirm a suspicion that the cocktail helps the barberpole worm digest its host's red blood cells. They're also trying to purify the cocktail's active ingredients so the size, molecular structure, and function can be described.

Fetterer refers to a key group of proteins as hemolytic factors (HFs). He believes the proteins are localized within membranes of the parasite's gut. There, like "molecular drill bits," they punch holes into the walls of ingested blood cells, causing hemoglobin to seep out.

KEITH WELLER (K8232-1)

Zoologist Ray Fetterer and technician Ruth Barfield draw a sheep's blood sample for analysis to see how the brown stomach worm causes red blood cells to collapse and lose hemoglobin. The goal is to develop an antibody to this parasitic nematode's hemolytic agent.

Millions of years of evolution have equipped the barberpole worm with a single, toothlike structure for scraping its host's stomach tissues to cause bleeding.

"It feeds by sucking up the blood, tissues, and anything that happens along," says Fetterer.

By secreting the HF proteins, he proposes, the parasite can then extract hemoglobin and other important nutrients from the blood cells.

Another player in the digestive process is the cysteine protease enzyme. "It helps break down the hemoglobin and other ingested proteins into smaller fragments," further aiding absorption, says Fetterer.

His lab is now conducting an informal study with scientists who are with Enzyme Systems Products in Livermore, California, to see if substances called inhibitors will obstruct cysteine protease activity in the barberpole worm. If so, the approach could deprive the parasite of a key nutrient-gathering tool.

Blood Busters

In addition to the barberpole worm, "some insects also have these types of enzymes," notes Fetterer. One such insect is the stable fly, from which researchers took their cue in searching for the barberpole worm's digestive cocktail. "If you just think about getting nutrients from a cell," says Fetterer, "then what you end up having to do is break it open."

The scientists began their search for that cell-breaking factor by grinding a barberpole worm's intestine and mixing a small amount of extract material with red blood cells from sheep. Normally, sheep red blood cells appear as smooth-surfaced disks with a slight dimple, or indentation, in the center. But exposing the cells to the parasite's hemolytic proteins quickly distorted their shape.

Images captured with a scanning electron microscope's high-powered eye revealed that the surface of the cells began to buckle after 15 minutes. By 30 minutes, jagged projections emerged, making the cellular surface appear harsh and alien. The cells also began losing hemoglobin, which escaped through holes that had opened up. By 90 minutes, the cells began to break apart, deflating as the last of the hemoglobin escaped.

"These observations support a hypothesis that the hemolytic factors serve as pore-forming agents," says Fetterer. "They insert themselves into red blood cell membranes, altering their structure and thus causing them to rupture.

"One of our goals," Fetterer continues, "is to further purify and characterize this hemolytic factor and see if we can develop an antibody to it."

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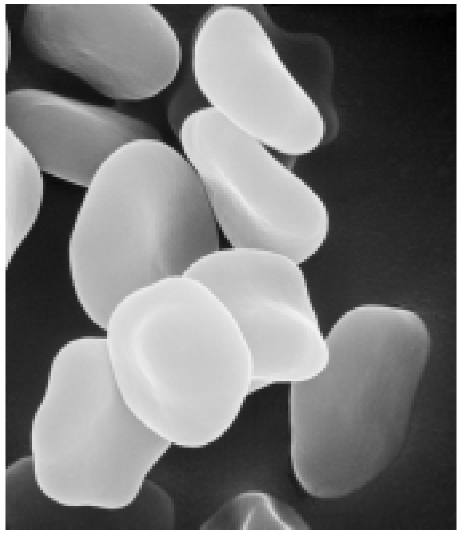

A scanning electron micrograph of a sheep's blood sample shows healthy red cells. Magnified about 6,000x.

Biochemical Benefactors?

An antibody also raises the prospect for developing a vaccine. Injected into a lamb, for example, a vaccine could help prime the young animal's immune system for nematode attack.

"There are no such vaccines currently available for controlling these parasites," says Fetterer.

Until then, anthelmintics—drugs that destroy or expel parasitic worms—will remain the staple defense. While effective, such chemotherapy isn't a magic bullet. That's because even a treated animal can reacquire the parasite by grazing on infected pasture, necessitating yet another round of treatment. To avoid this costly cycle, farmers must be diligent about where and when they put their animals out to graze.

Sheep are especially vulnerable to barberpole worm assaults. For one, sheep aren't averse to grazing pasture where manure is present that may contain parasite eggs, according to Virginia Cooperative Extension scientists in Blacksburg.

Sheep also graze plants close to their roots, where parasite larvae are most concentrated. To make matters worse, "the larvae are actually specialized at crawling up grass blades where they can be ingested," adds Fetterer.

Once ingested, parasite larvae quickly find their way into the host's abomasum, or true stomach. There, they mature, mate, and produce eggs in about 21 days.

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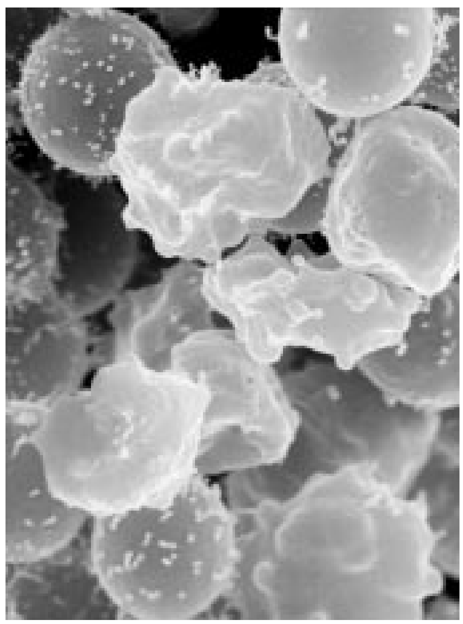

Red cells in blood of a sheep exposed to hemolytic proteins from barberpole worms are rough and misshapen. Magnified about 6,000x.

In susceptible or young animals, parasite numbers can build so high that the animal loses more blood than its body can replace. Severe blood loss can kill an animal, says Fetterer. Milder or chronic infections can cause lethargy and loss of appetite and can interfere with weight gain. This affects a producer's profit when animals show a drop in their milk, meat, or—in the case of sheep—wool production.

Setting the Stage for Parasite Sabotage

Fetterer's hope is that what is learned about the barberpole worm's key weaknesses will also apply to some other nematode parasites, like the brown stomach worm, *Ostertagia ostertagi*. In the United States, this parasite—more than the barberpole worm—is a menace to beef cattle, especially heifers and breeding stock.

"Ideally, we'd like to find something common to the Trichostrongylidae," says Fetterer. This nematode family includes *Haemonchus, Ostertagia*, and about a half dozen other species known to parasitize ruminant animals.

Next to antibiotics, administering anthelmintic drugs is often a farmer's second highest production cost, Fetterer says. So, "if you could reduce the reliance on chemotherapy, you could reduce costs." That's especially important in light of the barberpole worm's increasing drug resistance.

Additionally, organically grown produce, including milk and meat products, is becoming more popular with American consumers—all of which opens the door to novel methods for protecting livestock and farmers' profits.

"The long-term rationale for doing this research is to understand how nematodes survive and adapt to their hosts," says Fetterer. "Such knowledge can lead to the development of new tools for producers to use so they can choose what's best for their particular management styles."—By **Jan Suszkiw,** ARS.

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