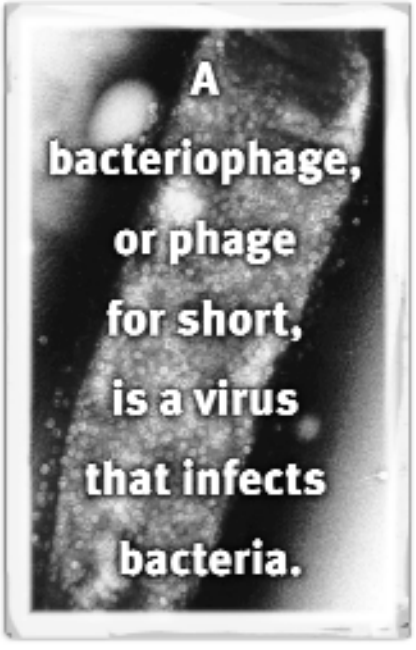
Antibiotic Alternatives

Bacteriophages offer promise of a practical solution for safe food and healthy animals.

Canadian researchers are one step closer to launching a new type of animal treatment with breakthrough potential to benefit the beef industry and beef consumers.

New "bacteriophage" treatments have unique advantages to protect cattle against major bacterial infections and provide an alternative to antibiotics, says Roger Johnson of the Public Health Agency of Canada. A bacteriophage, or phage for short, is a virus that infects bacteria.

Several phages, including ones targeted at *E. coli* O157:H7, are performing well in advanced testing and could result in products on the market within three to five years. Other phages targeting *Salmonella typhimurium* DT 104 also have potential. Early research with these phages was supported by the Canada Alberta Beef Industry Development Fund (CABIDF).



"The *E. coli* O157:H7 phages we're testing are producing very promising results," Johnson says. "Safety and efficacy results look very satisfactory, and we're working toward optimal formulations and delivery systems. We're optimistic this work will result in valuable animal treatment options that will be practical and cost-effective for beef producers, and provide great food safety and perhaps animal health advantages."

Scientists have known about phages for 90 years, but as therapeutic agents, they have been largely placed on the back burner in the Western World ever since the discovery of antibiotics for the treatment of bacterial infections, Johnson says. Rising concerns related to overreliance on antibiotics and emergence of bacteria resistant to multiple antibiotics have sparked renewed interest internationally in developing phages as an alternative treatment.

"We have seen the emergence of new foodborne pathogens, such as *E. coli* O157:H7, that are difficult to control," Johnson says. "We have also encountered microorganisms that have rapidly developed resistance to many antibiotics, *Salmonella typhimurium* DT 104 being a prime example. As a result, there is strong interest in exploring avenues that could replace antibiotics under these circumstances."

In the question-and-answer session below, Johnson provides a big-picture outlook of the prospects for phages, including benefits for beef producers.

What is the current stage of progress toward a bacteriophage treatment for* E. coli *O157:H7 and* S. typhimurium *DT 104, and what are the key obstacles ahead?

The keys here are to ensure the dosage that reaches the intestinal tract of cattle is effective, that the viability of the phages is preserved, and that we can provide the phages in a form that is easy for cattle producers to administer.

We're hopeful we can develop a relatively dry product that could be added to cattle rations as a granular powder. Such a formulation would survive well and would be dense enough to not blow around in the field.

Once this work is near completion, the next step is applying for regulatory approval to conduct a field trial with these phages in naturally raised cattle. It would probably take one whole summer to do the trial, and then another year to put the data together. If that is successful and the indications are good, it would probably be another two or three years before there would be a product on the market. We're looking at another three to five years.

What are the key questions to ensure the safety of this approach?

There are a lot of questions we consider important. For example, are the phages we selected able to transfer undesirable genes from one bacterium to another — a process called transduction?

Another question we've examined is whether there would be any detrimental effect on humans if these phages were used in cattle and got into the meat supply. So far, what we're finding is good news. The phages we've selected have a very low frequency of transduction, and we haven't found any evidence that they switch on key genes in affecting virulence for humans.

Will phage therapy be practical for cattle producers?

When it comes to production for commercial use, we don't want to have to be handling a potent human pathogen. There would be regulatory issues on the oral administration of a product to cattle that was derived from bacteria cultured in medium that might contain animal products. We have gone to a plant-based media and these nonpathogenic hosts to avoid those issues.

Aside from being an alternative tool, what is the key advantage of phages?

One very appealing feature is that phages are easy and economical to produce in large quantities. Also, phages are unique because they actually evolve in response to changes in their target bacteria. But, unlike antibiotics, phages respond to finding that their host has become resistant by mutating themselves so that they can reinfect the new type of bacterium.

How would you describe the evolution of bacteriophage research?

Since phages were first discovered in the early 20th century, there's been a lot of excellent work done in Eastern Europe, Poland, Russia, the Czech Republic and especially in the Republic of Georgia. Those regions frequently use these kinds of therapies in people. The Eliava Institute in the Republic of Georgia is named after George Eliava who, with Felix D'Herelle, a French Canadian, first developed phages for therapeutic use in humans.

In the West, the application of bacteriophage therapy in animal health and food safety goes back to work of Hugh Williams-Smith in the late 1970s in the United Kingdom (UK).

Editor's Note: *Adapted from a Meristem Land and Science release. To see the release in full, visit* www.meristem.com/topstories/ts06_08.html.