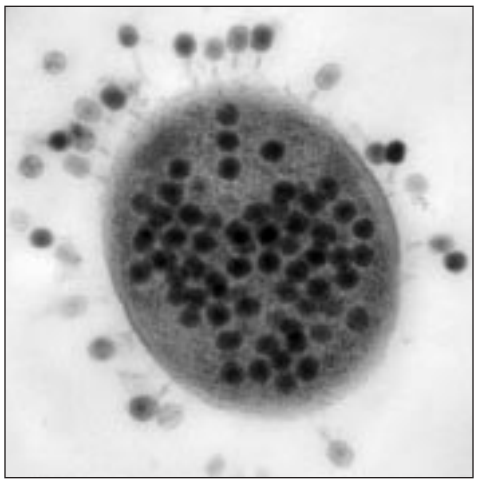
Bacteriophage: an old weapon against bacteria reemployed

Strains of bacteria resistant to most available antibiotics have raised the possibility that veterinary medicine may soon be confronted with untreatable bacterial infections. Researchers are looking for other treatments of such infections and are investigating the use of bacteriophage (phagin: Greek, to eat) to combat bacterial infection.

Bacteriophage are small viruses that infect bacteria and kill them by multiplying and basically filling the bacterial cell to bursting. They don't affect the infected host, because bacteriophage activity ceases once the bacterial cells are killed. Bacteriophage, which exist in many varieties, do not attack bacteria indiscriminately, they each usually attack only one specific kind.

Dr. Charles Benson, professor of microbiology, is working on utilizing bacteriophage to treat bacterial infections in dairy cows. He has identified several phage that work against specific organisms causing infections.

Bacteriophage were discovered accidentally early in the 20th century by Frederick W. Twort, working at the Brown Institution (London), who was looking for filterable agents that were nonpathogenic virus. He reported them in *Lancet* as the filterable agent that had preferential activity against micrococci. The speculation offered was that nonpathogenic viruses grew in bacteria while the pathogenic strains grew in animals. In 1917, Felix d'Herelle rediscovered Twort's lytic principle. d'Herelle had isolated his agent from cultures of patients with bacillary dysentery (shigellosis) and concluded that the filterable agent was an obligate bacteriophage. He proposed and utilized these bacteriophage as "true microbes of immunity" in therapies. His work continued for years up to his death in 1949. Twort, having never been seriously involved with phage therapy nor properly credited for his initial observations, died in 1950. Sinclair Lewis fictionalized the use of bacteriophage as a therapeutic agent in his 1926 book entitled "Arrowsmith."



Bacteriophage

The study of bacteriophage during the 40's through to present day has lead to a number of observations that suggest reconsideration of phage therapy might provide a mechanism for circumventing the rising concerns about the growing spectrum of resistance to antibiotics by using a new approach. "In actuality, the approach is not new but an old process to be revisited and modified based on the discoveries since Twort and d'Herelle presented their initial findings," says Dr. Benson. "There are many advantages: to name a few, the cost of isolating and preparing phage solutions is considerably less than the discovery and production of antibiotics, cost of testing the activity of the phage against a pathogen is much lower than defining antibiotic activity spectrum, phage are not harmful to the animal, resistance to phage does not impact on human health medicine as does the developing resistance of the pathogen in the animal to the drug and, an important factor, there are no significant withdrawal times involved when phage are used to treat a disease in food animals."

Dr. Benson has treated seven cows with *Pseudomonas aeruginosa* mastitis. In all instances the mastitis infection was resolved although experimental and collaboration difficulties prevented following the animals through the drying-off period. More recently, Dr. Benson has collaborated with **Dr. Michaela Kristula** to evaluate and experimentally treat *Staphylococcus* mastitis in cows in the Marshak dairy herd. They have experienced success but not to the extent that Dr. Benson had anticipated and he is working now to modify the preparation to provide Dr. Kristula with a more effective solution.

V.M.D./ Ph.D. program

Penn's NIH-supported VMD-PhD program was initiated in 1969 and is the only such program in the nation. Penn's School of Medicine offers an NIH-funded MD-PhD and veterinary and medical students attend many of the same lectures and courses and interact in research laboratories on campus. The program is highly competitive and each year only one or two students are admitted (although plans are in place to expand the program). The School is providing limited, additional funds to attract more students as there is a great need for veterinary medical researchers at universities, in industry and government agencies.

Since its inception, the program has graduated 47 individuals. It generally takes seven to eight years to complete the program. In the VMD curriculum students receive a thorough training in the basic sciences as they relate to veterinary medicine. They are exposed to and involved in scientific research through the Graduate Groups at the University and can select courses in any one of the following subjects: biochemistry and molecular biophysics, cell and molecular biology, epidemiology and biostatistics, genomics and computational biology, immunology, neuroscience, parasitology, pharmacological sciences, biology, and bioengineering. They are able to participate in research projects with outstanding scientists across the University. The VMD-PhD students also receive training in clinical medicine as they rotate through the clinical services at the two hospitals.

After completion of the program, about fifty per cent of the graduates go into internships or residencies, and the balance pursue postdoctoral training. Of the 47 graduates of the program, eighty-five percent are pursuing careers in research: 26 serve on academic faculties, seven of these are chair, chief or head of a department; six are active in the pharmaceutical industry, three as directors and two as presidents of companies; seven are postdoctoral fellows, interns, or residents; two are on clinical faculties; one is with a government health agency; and five are in private practice.

Currently there are 14 students in various stages of the program. Four new students joined the program in the 2002 academic year. The School would like to expand the program to at least five to six new students each year as there is a great need for medically trained researchers. What hampers the expansion of the program is lack of funds, as these students need financial support to complete the program. Ideally, the School would like to provide full funding for each student, and efforts are underway to secure the funds needed for this goal.