PHAGE THERAPY - ON THE THRESHOLD OF LIFE WHERE CHEMISTRY AND BIOLOGY MEET TO CONQUER SUPERBUGS.

According to the recent book by Shnayerson, M.; M.J. Plotkin entitled The Killers Within - The Deadly Rise of Drug-Resistant Bacteria, Little, Brown and Company, N.Y. ISBN:0-316-71331-7, about 40,000 North Americans die each year because of antibiotic-resistant infections — that amounts to about 110 per day. Some experts state that we are on the road to an impending public health crisis where the increasing incidence of antibiotic-resistant superbug infections threaten many medical procedures, unless new or alternatives to antibiotics become available. Yet phage therapy products are commercially available and used to successfully treat such infections in Georgia (Eastern Europe), Poland and Russia.

If one clicks http://www.phagetherapy.com the following statement welcomes visitors - "One of the most exiting developments in combating disease is Phage Therapy. Join us in the exploration of this fast breaking field." From cures of antibiotic-resistant infections, to 95% reductions of Salmonella strains in poultry, to a potential cure for *Vibrio vulnificus* infection from eating raw oysters, to a treatment for anthrax (see - http://www.sciencedaily.com/releases/2002/08/020822070131.htm for an example of phage enzyme therapy **)**
, and the eradication of *E. coli O157:H7*, phage therapy seems to provide an answer.

Bactericidal, heat-labile, lytic principles in rivers in India were discovered in the 1890's and it was subsequently confirmed that many rivers with fecal pollution contained similar bactericidal agents. Tanner, in his classic text book, Food Microbiology (1944), examines this phenomenon in some detail; however, it was d'Herelle in 1917 who demonstrated that the bacteria-lytic activity was due to viruses which were parasitic for specific for bacteria - he named them bacteriophages or phages - "bacteria eaters." Phages, like all viruses, are complex chemical entities consisting of a nucleic acid core covered by a protein coat and they may have contractile tail structures; however, they have no independent means of reproduction. However, the presence **of the right strain of bacteria presents the opportunity for phages to fulfil their life cycle and raison d'être and excite the reproductive machinery of the phages into action. In stealth, moon lander fashion phage soon attaches to a suitable host bacterium, injects it's DNA which commandeers the reproductive system of the host bacterium and in a short time (30 minutes) the bacterial cell bursts open releasing more than 200 copies of phage, each looking for a new host to conquer -- considering that bacteria multiply by dividing in two, while phage produces about 200 offspring for every bacterium killed, clearly with those odds even superbugs are superbugs no more and look more like victims -- all this is simply to say, that what a cat is to a mouse, the right phage is to a superbug.**

Until 1940 Phage Therapy was widely practised and researched, often with contradictory results, mainly because the biology of bacteriophages was poorly understood. With the introduction of antibiotics

phage therapy was essentially abandoned in the West until the 1980's when antibiotic-resistant, superbug infections caused some Western scientists to reexamine the potential of phage to cure human and animal infections, as well as their potential for reducing or eliminating contamination from foods, ranging from vegetables to meats.

Meanwhile, d'Herelle helped establish the Elivia Institute of Bacteriophage, Microbiology, and Virology in Tbilisi, Georgia which opened in 1923. This institute became the main supplier of a broad range of phage therapy products throughout the former Soviet Union.

In 1997 Dr. Elizabeth Kutter from Evergreen State College, in Olympia, Washington examined the state of phage therapy mainly in the former Soviet Union/Georgia in her comprehensive review entitled , Phage Therapy: Bacteriophages as Antibiotics -
(http://www.evergreen.edu/phage).

At present, in addition to established organizations in Georgia, Russia and Poland which are reportedly marketing therapeutic and prophylactic phage products against bacteria including Staphylococci, Streptococci, *E. coli*, Pseudomonas, Proteus, Salmonella, Shigella, Serratia, Klebsiella, Enterobacter, Campylobacter, Yersinia and Brucella, there are about twenty companies world-wide racing to bring phage therapy products for a range of medical, animal husbandry, food processing and environmental applications to market. Some examples are: USA (Intralytix, Inc - http://www.intralytix.com), Canada, India (**GangaGen - www.gangagen.com), Germany - (http://www.bacteriophage.net), and Israel (Phage Biotech Ltd - http://www.phage-biotech.com)** It is anticipated that the first phage-based product(s) will receive FDA approval in 2003; an "experimental use permit" from EPA has been granted for use of phage in the environment on non-food contact surfaces. This presentation is designed to provide an appreciation of the history of phage therapy, explore it's potential to treat antibiotic-resistant superbug infections and provide an overview of industrial and academic research, as well as an overview of the regulatory situation.

Prepared by G.W. (Bill) Riedel, PhD, 42 Richlin Cres., Ottawa, On, Canada K2B 8K4
Tel: 613-828-5756 - Email: briedel@magma.ca