Bacteriophage therapy offers new hope for streptococcal infections

Bacteriophages can be used to eradicate the carriage of pathogenic group A streptococci without destroying the normal microflora in the mucosal membrane, according to a study by Daniel Nelson and colleagues. (*Proc Natl Acad Sci USA* 2001; 7: 4107–12). "We believe that for the first time since the advent of antibiotics, we may have an alternative strategy to kill bacteria using highly evolved enzymes that have been developed by bacteriophages to kill bacteria", says Vincent Fischetti, a lead investigator of the study (Rockefeller Institute, New York, USA).

Bacteriophages are viruses that infect only bacteria. Each kind of bacteria has a corresponding bacteriophage (or "phage") that infects it. In streptococci, the phage replicates and the progeny phage produce enzymes, which are used to degrade the bacterial cell wall (killing the micro-organism in the process) so they can escape and infect other nearby bacteria.

The researchers examined the killing activity of one of these enzymes on group A streptococci using a murine hydrolase, referred to as lysin, from the streptococcal bacteriophage C1.

The researchers believe the enzyme acts on contact with the bacteria. Within 5 s, 1 000 units (10 ng) of enzyme were able to kill a 10^7 culture of group A streptococci in vitro. Furthermore, when the researchers orally treated nine colonised rats with lysin (500 units), they found the enzyme eliminated group A streptocccoci 2 h after treatment.

Since colonising streptococci are generally exposed on human mucosal epithelial surfaces in much the same way as in mice, the investigators are confident they will see the same results in human beings.

Pre-treating mice with lysin (250 units) prior to infection significantly protects the mice from colonisation compared with the control mice with no lysin. In addition, unlike traditional antibiotics, the researchers showed that giving C1 phage lysin does not harm the indigenous mucosal bacteria. "The use of phage lytic enzymes offers a safe alternative [to antibiotics]. It may also be used to prevent the spread of streptococci to classmates and family members if the infected individual is treated orally with the enzyme", Fischetti adds.

One area where the therapy could be invaluable is in developing countries, say the authors, where "strep throat" can lead to rheumatic fever, a major cause of heart disease in childhood. The US army are also interested in controlling streptococcal infections among recruits.

The team plans to begin phase I clinical trials on the streptococcal enzyme. "We are also in the process of developing enzymes for pneumococci to control otitis media in children and pneumonia in the elderly, because the penumoccoci that cause these diseases are carried in the nasopharynx prior to infection. Lowering their numbers in the nasopharynx, will result in a major impact on these diseases", Fischetti concludes.

Pam Das