

# Treatment with Bacteriophages of Experimentally-Infected Mice Caused by Antibiotic-Resistant *Pseudomonas Aeruginosa*

Dear Editor,

After discovery of bacteriophages, a great deal of faith was placed on their use for treatment of bacterial infections.<sup>1</sup> However, by administration of antibiotics, use of phage as antibacterial agent has been ignored.<sup>2</sup> After many years, the idea of phage therapy and prophylaxis was renewed recently because of increasing antibiotic resistance.<sup>3</sup> In this study we have investigated the potential of phages for the treatment of *Pseudomonas aeruginosa* infection in mice.

A strain of *P. aeruginosa* was used which was resistant to many of routinely-used antibiotics. Bacteriophage was originally isolated from sewage by standard methods using mentioned strain of *P. aeruginosa* as host.<sup>4,5</sup> Pathogen-free mice were chosen at 3<sup>rd</sup> wks of age. First approximate lethal dose 50% of this strain of *P. aeruginosa* were surveyed (around 10<sup>5</sup> CFU). In our experiment, we used a much higher dose (10<sup>7</sup> CFU) so that it could kill 100% of non-treated mice. Two groups of 10 mice (case and control) were inoculated intraperitoneally with 10<sup>7</sup> CFU of *P. aeruginosa*. In the case group, 10<sup>9</sup> PFU of phage particles was inoculated into peritoneal cavity, at the meantime and every 12h up to 4 doses.

After inoculation of mice with 10<sup>7</sup> CFU of *P. aeruginosa*, they became ill and eventually, collapsed within 24h of inoculation. When both *P. aeruginosa* and phage (10<sup>7</sup> CFU of bacteria and 10<sup>9</sup> PFU of phage) were administered simultaneously followed by 4 other doses of 10<sup>9</sup> PFU of phage every 12h, no mortality was observed at all. The numbers of dead mice in the control and treated groups were 10 and 0, respectively. We concluded that in mice which inoculated with *P. aeruginosa*, bacteriophage administration showed significant protection against mortality.

Studying the kinetics of bacterium and phage multiplication in these mice showed that in the absence of phage the *P. aeruginosa* multiplied in mice almost as fast as in broth culture. When phage was given to these mice intraperitoneally, the phage multiplied rapidly on the bacteria and prevented massive multiplication, resulting in a decline in bacterial numbers.

This study have confirmed that a bacteriophage which is active and lytic *in vitro* against *P. aeruginosa* was very effective in preventing and treating peritonitis with this strain in mice. Although the sample sized used in this study was not large, it seems likely that the use of phage in mice is able to control infection. The results indicate that bacteriophages have the potential for the prevention and/or treatment of certain bacterial infections of animals and of humans, at large. Further experiences are warranted to clear the role of phage in phagtherapy and prophylaxis for infection. Because of the increasing problems of bacterial disease and bacterial antibiotic resistance worldwide, it would seem timely to begin to look afresh at this approach and begin a period of renewed and rational assessment.

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