

## BOOK REVIEW

### 1. Molecular epidemiology of bacterial infectious disease in an age of rapid DNA sequencing and the Internet

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### 2. Phage therapy: bacteriophage as natural, self-replicating and self-limiting antibiotics

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Reviewed by J. GOWRISHANKAR\*

The two monographs under review are transcripts of two of the Sune Bergström Public Lecture series, delivered in Bangalore by the authors in 2000 and 2001 respectively, under the aegis of the AstraZeneca Research Foundation India. Both address the issue of bacterial infectious diseases and their control, a subject of considerable interest to the activities of the Research Foundation and, of course, of immense relevance to India.

Of the two, the lecture by Kutter is the more provocative in that it discusses a potentially useful alternative, namely phage therapy, to the more traditional approach of antibiotic administration in the management of bacterial infections. As she lucidly explains, the concept of phage therapy is neither novel nor untested. Indeed, the idea was around ever since phages were discovered in the early years of the last century, and was to become the major theme of research of one of the discoverers, Felix d'Herelle. The results obtained by these pioneers (many of whom worked in India) were also quite impressive, and while reading the monograph this reviewer was left contemplating on the possible reasons why phage therapy subsequently 'largely faded into oblivion', at least in the Western countries, after the Second World War. Was it the advent of antibiotics as 'wonder drugs'? Or was it, as the author suggests, that '[W]ith the increasingly complex political scene in India and in Europe . . . , funding for the Bacteriophage Inquiry was dropped in 1935 and few outside of India were aware of the study'? Or could it have been yet another innocent victim of the Cold War, since phage therapy was (and continues to be) extensively used in countries of the Eastern Bloc and hence the West would have nothing to do with it? Perhaps too, it was a combination of all of these reasons.

Kutter then goes on to describe the general biology and lifestyle characteristics of the bacteriophages (in particular

of coliphage T4, which has been extensively studied by her group), and the rationale underlying renewed interest in their use as antibacterial therapeutics. Potentially, the most important advantage with phage therapy is its exquisite specificity and absence of 'broad-spectrum' activity. Joshua Lederberg has also recently written a brief commentary on this subject (Lederberg J. 1996 Smaller fleas . . . *ad infinitum*: therapeutic bacteriophage redux. *Proc. Natl. Acad. Sci. USA* **93**, 3167–3168). The summary of their message appears to be that phage therapy holds considerable promise as an alternative to antibiotics, and that its use needs further investigation. A recent paper (Bernhardt T. G., Wang I.-N., Struck D. K. and Young R. 2001 A protein antibiotic in the phage *Qb* virion: diversity in lysis targets. *Science* **292**, 2326–2329) also hints at the possibility of using phage-encoded gene products in the treatment of bacterial infections. Incidentally, Kutter explains why the two alternative modes of therapy (phage and antibiotics) are mutually exclusive, since phage need living bacterial host cells to increase their own numbers.

Spratt's monograph describes means to undertake epidemiologic studies of bacterial infections, and to determine the clonal relationships, if any, between organisms of a single species causing outbreaks of disease at diverse locations. In this, he discusses in detail his own group's pioneering efforts to develop and standardize the technique of multilocus sequence typing (MLST) as an improvement on the more traditional approach of multilocus enzyme electrophoresis (MLEE) for epidemiologic studies. Although both approaches are equally effective in distinguishing between various nonclonal isolates, the former has the advantage that data from different laboratories can easily be integrated into a single database and transmitted over the World Wide Web. Spratt also points out the contribution of horizontal gene transfer and of recombination in the generation of non-clonal populations, a subject of substantial interest in its own right in light of both its evolutionary implications

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and the recent elucidation of the role of mismatch repair genes in the process (Denamur E., Lecointre G., Darlu P., Tenailon O., Acquaviva C., Sayada C., Sunjevaric I., Rothstein R., Elion J., Taddei F., Radman M. and Matic I. 2000 Evolutionary implications of the frequent horizontal transfer of mismatch repair genes. *Cell* **103**, 711–721).

In summary, both monographs represent good overviews of emerging areas in the field of studies on infectious disease. Since both represent verbatim reproductions of the lectures delivered, the style of presentation is very ‘conversational’, which this reviewer found somewhat distracting, and one may hope that the Foundation in future would rectify this shortcoming.