Correspondence

Pneumococcal Serotypes and Virulence

To the Editor—Pneumococcus is a venerable microorganism with an amazingly rich history. Those of us who study this organism should constantly examine our present findings in light of the wealth of previous literature. I am concerned when investigators draw conclusions from their own excellent but potentially limited data without referring to or noting discrepancies with that earlier body of knowledge.

A case in point is the recent article by Sandgren et al. [1], on the virulence of pneumococci. The authors state that type 1 pneumococcal infection in humans is associated with a low mortality. Of the 4 references that they cite to support this statement [2–5], only 1 [4] actually provides data, and it bases this conclusion on a study of 12 isolates, the source of which was not stated.

In contrast, Heffron [6] cites 11 studies from the preantibiotic era in which the overall mortality due to type 1 lobar pneumonia was 58% (range, 14%–82%) in 351 bacteremic cases and 15% (range, 3%–23%) in 457 cases of nonbacteremic disease. The variability from one report to the next is interesting, because it shows the importance of citing broadly rather than narrowly, but one can hardly conclude that type 1 pneumococcus is not highly virulent in humans. Similarly, in the antibiotic era, Austrian and Gold [7] found a mortality of only 8% in bacteremic type 1 pneumonia, but Calder et al. [8] recorded 2 deaths in 7 cases, and Mufson et al. [9] noted 6 deaths in 21 cases. The characterization of these cases as being type 1 came about because this was the first strain that the Klemperers systematically studied; it could have been an accident but was not. In the recent epidemic of type 1 pneumococcal meningitis [10], the mortality was 44%.

Nearly all the references cited in a recent article by Sandgren et al. [1] were from the preceding decade, most from the preceding 5 years, and discrepancies between their findings and those reported in the earlier literature were simply not addressed. I am not proposing that we weigh down our articles with early references, but I do think that it is important for investigators to maintain a close familiarity with older literature and to either cite similarities or try to explain or resolve discordant results.

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References


Reply to Musher

To the Editor—The conclusions of my colleagues and I are based on studies that have been conducted during the past decade in the Western world. Of 29 individuals with invasive disease caused by type 1 pneumococcus whom we have observed, none have died; and this is in contrast to what we found for many other serotypes [1] in the antibiotic era. In addition, we have performed molecular typing of these isolates and have found that the type 1 isolates are genetically closely related, belonging to the same clonal cluster. In Sweden, we have seen, between 1992 and 1997, an increase in the number of type 1 isolates, and, to a large extent, this increase was due to the emergence of one clone belonging to this cluster. From other unpublished studies, we know that representatives of this clonal cluster of type 1 pneumococcal pneumonia are widespread in the United States and that representative strains have been observed in many of the countries where surveillance has been performed. It is possible that outbreaks of type 2 pneumococcal disease will be observed as a result of increased vaccination rates. Further work in the field is needed in order to determine the role of pneumococcus type 2 disease, which represents a large proportion of pneumococcal disease in the United States, but which has been largely neglected in the past.
mococcus lack a pathogenicity island that is present in the genome of several other pneumococci.

One possibility is that the type 1 strains to which Musher refers might be more virulent because their genetic makeup is different than that of the clonal types that we have studied. The recent report by Leimkugel et al. [2], of a study in Ghana, was published while our report was in press, and what they found was that an outbreak of pneumococcal meningitis was caused by type 1 isolates with ST217 and its 2 single-locus variants, ST303 and ST612, and that this outbreak had a lethal outcome. These are not the same clones that we found, which suggests that the clonal type might be a very important determinant of disease outcome. In addition, treatment strategies and host susceptibility in Ghana might have an important effect on disease outcome. If pneumococcal isolates from the preantibiotic era are still available, we would be most happy to characterize them further.

In our studies in mice [3], we found that the type 1 strain belonging to the clonal cluster described above exhibits a low cytokine response—in contrast to the TIGR4 strain, for example. Whether this low cytokine response also occurs in humans remains to be shown. However, an interesting possibility is that mortality associated with type 1 isolates during the preantibiotic era could have resulted from bacterial overgrowth due to a deficient innate immune response. One would expect that invasive pneumococcal disease with a less pronounced degree of inflammation would be easier to treat with antibacterial agents, compared with treatment of pneumococcal infections that have a high degree of inflammation and that have a mortality that may reflect the host response more than the bacterial growth. We thank Musher for bringing this interesting possibility to light.

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**References**


Potential conflicts of interest: none reported.