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Correspondence

Anti-endotoxin immunotherapy in septic shock

Sir,

In his leading article on this subject (Cohen, 1986) Dr J. Cohen made the following statement, reported as a personal communication from M. P. Glauser: "Furthermore, reexamination of the data from the original study by Ziegler *et al.* (1982), suggests that protection from shock was related to the generation of the highly conserved Re antibodies, rather than the Rc core associated with *E. coli* J5". In fact, M. P. Glauser never reported unpublished data from Ziegler's study. The mistake was probably a misunderstanding of part of a paper given at the IXth International Congress of Infectious and Parasitic Diseases, Munich, 1986, in which M. P. Glauser reported data from in-vitro studies performed in rabbits by one of us (J. D. Baumgartner) in collaboration with Dr E. Ziegler. These data revealed that immunization of rabbits with *Escherichia coli* J5 produced antibodies of two types: (1) antibodies to J5 core determinants distal to KDO, which were mainly type-specific and were quantitatively predominant, and (2) antibodies to the lipid A-KDO region, which were less abundant, but highly cross-reactive (Baumgartner *et al.*, 1987). The latter antibodies were measured with Re LPS as antigen, since Re LPS is composed only of lipid A and KDO, in contrast to J5 LPS which possesses several additional core sugars. Thus, although these in-vitro results suggest that antibodies to lipid A-KDO are more likely to afford cross-protection after immunization with *E. coli* J5 than antibodies to J5 LPS core sugars, this has not been demonstrated clinically.

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References

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Determining the MICs of β-lactams for *Haemophilus*.

Sir,

With regard to Dr Yourassowsky and colleagues' suggestion that the data regarding *Haemophilus influenzae* in our recent publication (Aldridge, Sanders & Marier, 1986) are artefactual, we have the following comments. We are aware of the pitfalls which exist with the broth microdilution method when studying increased inoculum sizes. Whenever our laboratory performs inoculum effect studies we routinely culture 10 μl of the 100 μl in each well. The growth or no growth of organisms is then used in those cases of questionable MICs to establish if viable organisms are present. With reference to the *H. influenzae* data in question, where an inoculum effect was evident the growth of viable organisms was demonstrated in all cases. The MBC determinations were not reported because no standardized MBC method has yet been approved in the United States.

We remind Yourassowsky *et al.* that the inoculum effect with ampicillin has been described with β-lactamase positive and negative strains of *H. influenzae* at inoculum sizes equal to or greater than 10^6 cfu/ml (Thornsberry & Kirven, 1974). Thus with an inoculum size of 10^6 cfu/ml, even in the presence of a β-lactamase inhibitor, it is not surprising, as in our study to see a significant inoculum effect since this has been described for β-lactamase negative strains. In addition a number of reports have described a significant inoculum effect when testing cephalosporins against β-lactamase positive and negative strains of *H. influenzae* (Jones & Preston, 1983; Bell & Washington, 1977).

In our experience doing susceptibility testing of *H. influenzae* by the broth microdilution has not produced excessive problems in MIC endpoint determination nor have we had problems reproducing results. As a matter of fact the use of the broth microdilution method for susceptibility testing of *H. influenzae* has been sanctioned by the National Committee for Clinical Laboratory Standards (1985) in the United States.

Finally, the differences seen between Yourassowsky and colleagues' results and ours cannot be adequately explained at this time.