Group A Streptococcal Pharyngitis and Penicillin G

To the Editor—In the December 2006 issue of Clinical Infectious Diseases, Kaplan et al. [1] presented in vitro experiments that support the well-known fact that penicillin does not penetrate into cells very well and, therefore, does not kill intracellular bacteria. Their experiments were made by selecting 16 virulent variants of several group A streptococcal (GAS) M types. They omitted studies of less virulent strains that remained within the host epithelial cells for >24 h. Their ingested virulent strains survived penicillin treatment for several hours but then disrupted the host cells. In contrast, the macrokines entered the host cells promptly, killing the GAS sooner, so that the host cells survived longer. What is the clinical significance of these findings to which the authors allude?

Undoubtedly, virulent GAS invade tissues and, when ingested and liberated from destroyed cells, they are (when proliferating) efficiently killed by penicillin G. According to all clinical, epidemiological, and microbiological evidence, penicillin is extremely effective in terminating clinical GAS infection. Perhaps these experiments reflect only the need to treat GAS pharyngitis for an adequate period of time (7–10 days) to prevent clinical relapses and sequelae, such as rheumatic fever. The real issue has been the possible significance of the post-therapeutic convalescent carriage of so-called “persisters” [2]. Unfortunately, the authors’ experiments did not compare the effect of antibiotics on intracellular strains of low virulence (unencapsulated and relatively low in M protein content), which may be internalized but may not destroy epithelial cells and which are characteristic of most of the stubborn persisters that have been studied by myself and others [2, 3]. For that reason, reculturing adequately treated GAS pharyngitis in the absence of clinical relapse has not been recommended and has not, to my knowledge, produced any clinically significant problems.

Moreover, Kaplan et al. [1] allude to the very interesting study of Medina et al. [4], which confirms the critical role of encapsulation in the ability of GAS strains to survive within polymorphonucleated WBCs long enough to destroy them. Again, except in cases of overwhelming infection, such transient intracellular survival does not seem to limit the effectiveness of penicillin G under conditions of natural human GAS infection. What is missing from current clinical investigation is (further) careful clinical evaluation of the strain virulence of “persisters,” of strains from asymptomatic carriers, and of strains from patients with low-grade (non-nexusudative) GAS pharyngitis, as presented years ago by others [5]. Until such evaluations are available—or until valid new clinical epidemiological evidence appears to challenge it—the priority of the use of penicillin G for the treatment of GAS pharyngitis should not be surrendered to the macrokines or to any other antibiotic.

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References


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Reply to Stollerman

To the Editor—Dr. Stollerman [1], a respected member of the streptococcal research community, has raised some issues that are important—but somewhat difficult to precisely define—about our data [2], the accompanying explanations, and