Relative Sensitivities of *Streptococcus pneumoniae* Strains to Penicillin and Ceftriaxone

Examining the data of Brueggemann et al. (1), we noticed that among strains of *Streptococcus pneumoniae* that are highly sensitive to penicillin, the sensitivities to penicillin usually exceeds the sensitivities to ceftriaxone (with MICs calculated in micrograms per milliliter). By contrast, among strains that are more resistant to penicillin, sensitivities to ceftriaxone more frequently exceed those to penicillin (Table 1). This finding emphasizes that mechanisms of resistance to different β -lactams differ among *Streptococcus pneumoniae* strains. Alter-

TABLE 1. Relative sensitivities to ceftriaxone of *Streptococcus pneumoniae* strains with various penicillin sensitivities^a

Penicillin MIC (μ g/ml)	No. of strains for which:			Total no. of strains tested	% of strains for which:		
	R < P	R = P	P < R		R < P	R = P	P < R
0.004	0	2	7	9	0	22.2	77.7
0.008	8	86	121	215	3.7	40.0	56.3
0.016	65	875	456	1,396	4.6	62.7	32.7
0.03	56	368	97	521	10.7	70.1	18.6
0.06	22	74	56	152	14.5	48.7	36.8
0.12	68	39	27	134	50.7	29.1	20.1
0.25	48	51	5	104	46.2	49.0	4.8
0.5	39	41	6	86	45.3	47.7	7.0
1	82	87	2	171	47.9	50.1	1.2
2	190	83	7	280	67.9	29.6	2.5
4	37	17	3	57	64.9	29.8	5.3

^a Data are from the study of Brueggemann et al. (1). Abbreviations: R < P, the ceftriaxone MIC was less than the penicillin MIC; R = P, the ceftriaxone MIC was equal to the penicillin MIC; P < R, the penicillin MIC was less than the ceftriaxone MIC.

ations in different penicillin-binding proteins (PBPs) have been implicated. Altered PBPs 1a, 2x, 2a, and 2b have been pinpointed in penicillin resistance (2–4, 6, 7), while altered PBPs 1a and 2x are characteristic of resistance to extended-spectrum cephalosporins (5). One can speculate that those PBPs that bind penicillin more avidly than ceftriaxone mediate the rate-limiting step in cell wall lysis under usual conditions but that, when these PBPs mutate and bind penicillin poorly, the PBPs that preferentially bind ceftriaxone become rate limiting. This hypothesis requires empirical verification.

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David S. Hodes
Thaddeus E. Sudol
Roche, USA
Nutley, New Jersey 07110-1199

Authors' Reply

Regarding the comments of Hodes and Sudol, we caution against overinterpretation of the minor differences between ceftriaxone and penicillin MICs for isolates of *Streptococcus pneumoniae* with low penicillin MICs. As they point out, in our study (1), ceftriaxone MICs for such strains tended to be slightly higher than penicillin MICs; however, the differences were small, i.e., usually ca. $1/2 \log_2$ dilution increment higher. It is not clear that this difference is meaningful or explained by different PPP binding affinities. We agree that such a hypothesis requires further investigation.

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Gary V. Doern
Michael Pfaller
Angela A. Brueggemann
Medical Microbiology Division
Department of Pathology
University of Iowa College
of Medicine
Iowa City, Iowa