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Barriers to Intravenous Penicillin Use for Treatment of Nonmeningitis Pneumococcal Disease▽

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Infectious disease physicians were surveyed to determine whether the new penicillin breakpoint change will translate into increased penicillin use and to identify barriers to intravenous (i.v.) penicillin use for pneumococcal infections. The inconvenience of i.v. penicillin may limit its use despite a reduction in numbers of infections considered resistant.

Streptococcus pneumoniae causes clinical syndromes, including bacteremia, peritonitis, and septic arthritis, and is the most common cause of bacterial meningitis and pneumonia in the United States. Penicillin breakpoints for pneumococcus were originally based on achievable penicillin concentrations in cerebrospinal fluid. However, penicillin achieves greater concentrations in the lungs and blood than in cerebrospinal fluid (1). In January 2008, new penicillin breakpoints for intravenous (i.v.) treatment of pneumococcal infections other than meningitis were published by the Clinical and Laboratory Standards Institute (CLSI) (3, 7). Based on these new breakpoints, many more nonmeningitis pneumococcal infections are now categorized as susceptible to penicillin (2, 7). Increased penicillin use might reduce the need for broader-spectrum antibiotics that increase the potential for antibiotic resistance (6).

Infectious Diseases Society of America (IDSA) guidelines for antimicrobial stewardship programs recommend using culture results to streamline or deescalate empirical antimicrobial therapy to more effectively target the causative pathogen, decrease antimicrobial exposure, and decrease costs (4). Except in an *IDSA News* article (5) and an updated package insert for i.v. penicillin produced by one manufacturer, the penicillin breakpoint change had not been widely publicized at the time that the survey was conducted. To determine whether the breakpoint change is likely to translate into increased penicillin use and to identify barriers to i.v. penicillin use for the treatment of pneumococcal infections, we surveyed infectious disease physician members of the IDSA Emerging Infections Network (EIN).

On 30 September 2008, 9 months following publication of the new penicillin breakpoints, a questionnaire was distributed via e-mail or facsimile to 1,247 adult and pediatric infectious disease physician members of the EIN and either the IDSA or the Pediatric Infectious Diseases Society. Members subscribe to an e-mail listserv for discussing topics related to the prevention, diagnosis, and treatment of infectious diseases. The 1-page introduction and 2-page self-administered questionnaire (both available upon request) containing 9 multiple-choice questions were developed with input from experts in the field of infectious disease. Topics covered in the questionnaire included awareness of the new penicillin breakpoint change, methods of learning about the breakpoint change, potential for change in prescribing practices, and barriers to i.v. penicillin use. The survey was redistributed to nonresponders twice over 3 weeks. Only respondents who reported that they care for patients with pneumococcal infections were included.

A descriptive analysis was performed on complete responses; denominators for certain questions varied, as not all physicians responded to all questions. Data were analyzed using SAS version 9.2. Comparisons between groups were made by chi-square analysis. P values of <0.05 were considered statistically significant.

A total of 588 responses were received (47% response rate). Characteristics of respondents, including patient population, practice setting, and residence, did not differ significantly from those of nonrespondents. Fifty-nine responses were excluded because the physicians reported that they did not treat patients with pneumococcal infection, leaving a final sample of 529 (42%).

We asked infectious disease physicians how they learned about the penicillin breakpoint change (Table 1). Of the 529 respondents, 82.0% were aware of the breakpoint change at the time of the survey. News reports from the IDSA, reports from clinical microbiology laboratories, and discussions with colleagues were the most common mechanisms for learning about the breakpoint changes. We asked the physicians how they would prefer to learn of similar breakpoint changes in the future. Preferred mechanisms included *IDSA News* reports, clinical microbiology laboratory reports, and documents published by the CLSI.

We then asked respondents to consider, given the breakpoint change, how likely they were and how likely they believed noninfectious disease physicians were to use i.v. penicillin when treating non-penicillin-allergic patients with pneumococcal infections. Over half of respondents reported that they

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TABLE 1. Method of learning about new penicillin breakpoints for i.v. treatment of pneumococcal infections[a]

Method of learning about new penicillin breakpoints	Current method		Preferred method	
	No. of respondents	%	No. of respondents	%
Society newsletter	273	51.6	297	56.1
Microbiology laboratory report	138	26.1	183	34.6
A colleague	128	24.2	76	14.4
This survey first	95	18	0	0
CLSI document	69	13	176	33.3
National conference	46	8.7	106	20

[a] Responses were not mutually exclusive.

were more likely to use i.v. penicillin (51.2%), while 11.1% reported that they believed that noninfectious disease physicians were more likely to use penicillin. "Don't know" accounted for 2.3% of responses from infectious disease physicians and 25.7% of responses regarding noninfectious disease physicians.

Table 2 shows infectious disease physician responses regarding reasons why they were unlikely and why they believed noninfectious disease physicians were unlikely to use i.v. penicillin for treating susceptible pneumococcal pneumonia. The most commonly reported barrier to i.v. penicillin use among infectious disease physicians was the frequent dosing schedule. Infectious disease physicians believed that the greatest barriers to i.v. penicillin use among noninfectious disease physicians were clinical improvement after the initial regimen, the convenience of continuing antibiotics that were started empirically, and confusing susceptibility reports.

Among 324 (61.2%) respondents who reported that their clinical microbiology laboratories report separate susceptibilities for meningitis and nonmeningitis pneumococcal isolates (as recommended by the CLSI), 28 (8.6%) rated laboratory interpretations as confusing. i.v. penicillin use has been encouraged at the institutional level according to 80 (15.1%) respondents.

Although awareness among infectious disease physicians about the 2008 i.v. penicillin breakpoint change for treatment of pneumococcal infections was high, it is likely that many fewer noninfectious disease physicians are aware of the breakpoint change. This is concerning, since most antibiotics are prescribed by noninfectious disease providers. Published reports from professional medical societies might help to increase awareness of the breakpoint changes. Communication via clinical microbiology laboratories and national conferences may also be effective for increasing awareness of penicillin and other antibiotic breakpoint changes in the future.

Approximately half of infectious disease physicians self-reported that they were more likely to treat patients with pneumococcal pneumonia with i.v. penicillin as a result of the change in breakpoints. According to the infectious disease providers surveyed, fewer noninfectious disease physicians were believed to be more likely to treat with i.v. penicillin. Barriers to i.v. penicillin use that are unrelated to concerns over antimicrobial resistance exist, so increasing awareness of breakpoint changes alone is likely insufficient to increase penicillin use.

Standard clinical practices are barriers to i.v. penicillin use. Many patients with pneumococcal pneumonia respond so well to initial empirical antibiotic therapy that by the time susceptibility results are available on the second or third hospital day, the patient has already been switched to oral antibiotics. Many physicians also find it more convenient to continue with empirical regimens than to switch to i.v. penicillin. Some antibiotics chosen for empirical therapy, such as ceftriaxone and fluoroquinolones, have the benefit of once-daily administration.

There are limitations to our evaluation. The response rate was 47%, and the population of EIN members who responded to the survey may not be representative of those who chose not to respond. The survey was limited to infectious disease specialists belonging to a professional medical society, and responses from our survey are not representative of the general population of physicians. Noninfectious disease physicians were not surveyed directly, so responses about this population of physicians may not be accurate. Awareness about the new penicillin breakpoints among infectious disease physicians likely increased following publication of an article, 8 months after the survey was conducted, that described the rationale for revising the breakpoints (7).

TABLE 2. Reported barriers to i.v. penicillin use for pneumococcal pneumonia treatment[a]

Response[b]	Infectious disease physician		Noninfectious disease physician[c]	
	No.	%	No.	%
No barriers	261	49.3	19	3.6
Frequent dosing	257	48.6	203	38.4
By the time susceptibility results are available, the patient has usually been switched to oral antibiotics	216	40.8	183	34.6
More convenient to maintain patients on empirical regimens recommended by the IDSA or hospital guidelines/formulary	96	18.1	247	46.7
Prefer not to change antibiotics if patient is improving on another i.v. antibiotic	90	17	341	64.5
Greater comfort with other antibiotics	59	11.2	154	29.1
Adverse events with i.v. penicillin	17	3.2	24	4.5
Susceptibility report confusing	10	1.9	220	41.6

[a] Responses from infectious diseases physicians regarding their own practice and their perceptions of practices of other physicians.
[b] Respondents were asked why they were unlikely to use i.v. penicillin to treat patients with pneumococcal pneumonia.
[c] Based on responses by infectious disease physicians.

Hospitals should ensure that clinicians are aware of the new penicillin breakpoint change for pneumococcal pneumonia. Antimicrobial stewardship programs should include strategies that ensure targeted antimicrobial therapy based on susceptibility results. If penicillin is to be used more often in these programs, steps need to be taken to make penicillin more convenient for clinicians, to provide instructions for penicillin use, and to enhance awareness and education about the importance of using narrow-spectrum agents. Rates of penicillin use in hospitals should be monitored to determine whether penicillin prescribing practices have increased since the breakpoint change and whether this change has had any impact on antibiotic-resistant, health care-associated infections. Penicillin use is unlikely to increase substantially without such interventions.

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