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Susceptibility Profiles of *Nocardia* Isolates Based on Current Taxonomy

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The genus *Nocardia* has undergone rapid taxonomic expansion in recent years, and an increasing number of species are recognized as human pathogens. Many established species have predictable antimicrobial susceptibility profiles, but sufficient information is often not available for recently described organisms. Additionally, the effectiveness of sulfonamides as first-line drugs for *Nocardia* has recently been questioned. This led us to review antimicrobial susceptibility patterns for a large number of molecularly identified clinical isolates. Susceptibility results were available for 1,299 isolates representing 39 different species or complexes, including 11 that were newly described, during a 6-year study period. All tested isolates were susceptible to linezolid. Resistance to trimethoprim-sulfamethoxazole (TMP-SMX) was rare (2%) except among *Nocardia pseudobrasiliensis* (31%) strains and strains of the *N. transvalensis* complex (19%). Imipenem susceptibility varied for *N. cyriacigeorgica* and *N. farcinica*, as did ceftriaxone susceptibility of the *N. nova* complex. Resistance to more than one of the most commonly used drugs (amikacin, ceftriaxone, TMP-SMX, and imipenem) was highest for *N. pseudobrasiliensis* (100%), *N. transvalensis* complex (83%), *N. farcinica* (68%), *N. puris* (57%), *N. brasiliensis* (51%), *N. aobensis* (50%), and *N. amikacinitolerans* (43%). Thus, while antimicrobial resistance can often be predicted, susceptibility testing should still be considered when combination therapy is warranted, for less well characterized species or those with variable susceptibility profiles, and for patients with TMP-SMX intolerance.

Nocardia species are ubiquitous environmental organisms that can cause a variety of diseases in humans. Clinical manifestations range from localized skin and soft tissue infection as a result of cutaneous trauma in otherwise healthy individuals to life-threatening pneumonia, central nervous system infection, and/or bacteremia in immunocompromised hosts. Recently, the genus *Nocardia* has undergone rapid taxonomic expansion as a result of the broad utilization of 16S sequencing for identification of clinical and environmental isolates. There are currently 86 recognized *Nocardia* spp., more than half of which have been described during the last 10 years, and most have been isolated from clinical specimens (1–3). Antimicrobial susceptibility profiles are predictable for several *Nocardia* spp. and have been used in the past to classify isolates into multiple distinct antibiotypes (4). Trimethoprim-sulfamethoxazole (TMP-SMX) has long been considered the therapeutic agent of choice for monotherapy, while combinations of TMP-SMX with amikacin, carbapenems, or ceftriaxone are often used for severe or systemic infections (1). Two recent surveys on sulfonamide-resistant *Nocardia* spp. in the United States provided conflicting information (5, 6). In addition, antimicrobial susceptibilities have not been systematically tested for several of the more recently described species. The purposes of this study were to review susceptibility data for a large number of *Nocardia* isolates identified using partial 16S rRNA gene (16S) sequencing in a national reference laboratory and to analyze antimicrobial susceptibility patterns based on current taxonomy.

MATERIALS AND METHODS

Clinical isolates were referred to ARUP Laboratories for identification and susceptibility testing from institutions throughout the United States. Isolates that were identified as *Nocardia* spp. by 16S sequencing between January 2006 and December 2011 were included in this study. Sequencing was performed using routine protocols (7), SmartGene analysis software (SmartGene, Raleigh, NC) (8), and Clinical and Laboratory Standards Institute (CLSI) guidelines (9). Chromatograms resulting from routine testing were reassembled with MicroSeq 500 software (version 2.0; Life Technologies, Grand Island, NY) for this study. Short (<400-bp) and low-quality (PHRED scores < 35) sequences were excluded. The remaining high-quality sequences were reanalyzed by comparison to type strain sequences of all valid *Nocardia* spp. (2, 3) using Geneious software (version 5.4.2; Biomatters). Isolates with <100% sequence identity to type strain sequences based on BLAST analysis (10) were compared to the NCBI nucleotide database using BLAST. Results were reviewed manually and interpreted using CLSI guidelines (9). Species that cannot reliably be differentiated based on partial 16S sequences were grouped into complexes (see Table S1 in the supplemental material). The *N. nova* complex was defined as previously reported (1) to include *N. africana*, *N. elegans*, *N. kruczakiae*, *N. nova*, and *N. veterana*. By partial 16S sequencing, the type strain of *N. mikamii* cannot be differentiated from those of *N. africana*, *N. elegans*, *N. kruczakiae*, and *N. veterana* using CLSI guidelines (9). Therefore, *N. mikamii* was also included in the *N. nova* complex for the purpose of this study. Since *N. nova* can be differentiated by 16S sequencing from the other members and is the most frequently isolated species of this complex, results are provided for isolates belonging to the larger complex and for *N. nova* itself. Isolates with sequence similarities of 99 to 99.5% to references were identified as *Nocardia* spp. and likely belong to yet-undescribed taxa.

Antimicrobial susceptibility testing (AST) was performed using com-

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TABLE 1 Antimicrobial nonsusceptibility for 1,299 *Nocardia* strains isolated over a 6-year period

Organism (*n*)	% of strains with result[a]										
	TMP-SXT R	AMK R	IMI R/I	CTR R/I	AUG R/I	LZD R	CIP R/I	CLA R/I	MIN R/I	TOB R/I	MXF R/I (*n*)
N. abscessus complex (110)	0	0	69	2	22	0	100	71	15	0	92 (39)
N. amamiensis (2)	0	0	0	0	50	0	100	100	0	0	100 (1)
N. amikacinitolerans (7)	0	57	28	43	0	0	100	86	14	0	100 (5)
N. aobensis (2)	0	0	50	50	100	0	100	0	100	100	100 (2)
N. asteroides sensu stricto (3)	0	0	0	0	100	0	100	100	33	0	100 (2)
N. beijingensis complex (30)	0	0	7	3	97	0	96	37	20	0	95 (18)
N. blacklockiae (1)	0	0	100	0	0	0	100	0	100	100	0 (1)
N. brasiliensis (148)	0	0	99	51	4.7	0	99	97	76	0	1 (88)
N. brevicatena (1)	0	0	0	0	100	0	100	0	0	0	0 (0)
N. carnea (2)	0	0	0	0	100	0	0	50	100	0	0 (0)
N. cyriacigeorgica (264)	0	0	57	12	97	0	100	99	94	0.8	96 (128)
N. exalbida complex (4)	0	0	25	0	100	0	75	50	50	0	100 (1)
N. farcinica (204)	0.5	0	67	97	24	0	57	99.5	95	99.5	21 (99)
N. flavorosea (1)	0	0	0	0	100	0	0	100	0	0	0 (1)
N. grenadensis (2)	0	0	100	0	100	0	0	100	50	0	0 (0)
N. higoensis (2)	0	0	50	0	100	0	0	50	0	0	0 (0)
N. ignorata (1)	0	0	100	100	100	0	100	0	0	0	0 (1)
N. mexicana (1)	0	0	100	0	100	0	100	0	100	100	0 (0)
N. neocaledoniensis (1)	0	0	0	0	100	0	100	100	100	0	100 (1)
N. niigatensis (2)	0	0	100	100	100	0	0	0	100	0	0 (1)
N. niwae (6)	0	0	0	0	100	0	100	50	50	0	0 (0)
N. nova complex (320)	0	0	1	53	91	0	99	3	88	87	98 (162)
N. nova[b] (246)	0	0	2	50	92	0	99	0	90	88	99 (132)
N. otitidiscaviarum (29)	0	0	93	100	100	0	93	93	55	38	65 (17)
N. paucivorans (11)	0	0	0	0	90	0	9	18	9	0	0 (5)
N. pseudobrasiliensis (13)	31	31	100	100	100	0	0	0	100	0	0 (7)
N. puris (7)	0	0	57	86	85	0	100	100	0	0	100 (1)
N. rhamnosiphila (4)	0	0	25	0	100	0	0	100	100	0	0 (2)
N. takedensis (1)	0	0	0	0	0	0	100	0	0	0	100 (1)
N. testacea (1)	0	0	0	0	100	0	0	100	100	0	0 (0)
N. thailandica (1)	0	0	0	0	100	0	100	0	100	0	0 (1)
N. transvalensis complex (83)	19	72	94	37	53	0	16	96	85	96	0 (41)
N. vermiculata (1)	0	0	0	0	100	0	100	0	100	0	0 (0)
N. vinacea (1)	0	0	0	0	100	0	100	0	100	0	0 (0)
N. yamanashiensis (1)	0	0	100	100	100	0	100	0	0	100	0 (1)
Nocardia sp. (32)	0	3	44	31	72	0	50	53	50	19	6 (16)
Total (1,299)	2	5	51	44	63	0	83	67	78	45	60 (642)

[a] Percent of strains with resistant (R) or intermediate (I) interpretation are listed. Testing for moxifloxacin was only available for a subset of isolates; numbers of strains are indicated in the last column. TMP-SMT, trimethoprim-sulfamethoxazole; AMK, amikacin; IMI, imipenem; CTR, ceftriaxone; AUG, amoxicillin-clavulanic acid; LZD, linezolid; CIP, ciprofloxacin; CLA, clarithromycin; MIN, minocycline; TOB, tobramycin; MXF, moxifloxacin.
[b] Antimicrobial nonsusceptibility results for the species *N. nova* are provided independently from those for the larger *N. nova* complex.

mercial broth microdilution panels (RAPMYCO panels; Thermo Scientific, Waltham, MA) only when requested by the treating physician. Briefly, organisms were resuspended in cation-adjusted Mueller-Hinton broth and inoculated at a final concentration of 1×10^4 to 5×10^4 CFU per well. MICs were determined for amikacin (AMK), amoxicillin/clavulanate (AUG), ceftriaxone (CTR), ciprofloxacin (CIP), clarithromycin (CLA), imipenem (IMI), linezolid (LZD), minocycline (MIN), moxifloxacin (MXF; 2009 to 2011 only), tigecycline (TGC; by request only), TMP-SMX, and tobramycin (TOB) and interpreted as recommended by CLSI (11). Epidemiological cutoff (ECOFF) values were estimated for tigecycline using two approaches: the first was defined as two doubling dilutions above the MIC_{50} and the second as two doubling dilutions above the modal MIC (12, 13). Both approaches yielded the same ECOFF.

RESULTS

A total of 2,198 isolates were identified as *Nocardia* spp. during the study period, 2,151 with species-level and 47 with genus-level identification (see Table S1 in the supplemental material). Isolates identified to the species level represented at least 37 different species or complexes. Thirty-eight species, including 15 that are part of complexes, were described since the year 2000, and 12 species were first described during the study period. More than 90% of isolates with species-level identification belonged to only 7 species or complexes (*N. nova* complex, *N. cyriacigeorgica*, *N. farcinica*, *N. brasiliensis*, *N. abscessus* complex, *N. transvalensis* complex, and *N. beijingensis* complex). It is important to note that *N. asteroides sensu stricto* was isolated very infrequently from patient samples. Only 4 isolates were identified during this 6-year study (0.2% of all isolates). Isolates were cultured from patients in 40 U.S. states, 47% of the patients were female, and the median age was 63 years. Most isolates were from respiratory (54%) or subcutaneous/cutaneous sources (26%), followed by blood (6%) or other body fluids

TABLE 2 MIC_{50} and MIC_{90} for TMP-SMX, imipenem, ceftriaxone, and amikacin for the 8 most common species[a]

Organism (*n*)	TMP-SMX		Imipenem		Ceftriaxone		Amikacin	
	MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}
N. abscessus complex (110)	≤0.25/4.8	0.5/9.5	**16**	**64**	**≤4**	**≤4**	≤1	≤1
N. beijingensis complex (30)	≤0.25/4.9	0.5/9.6	≤2	4	**≤4**	**≤4**	≤1	≤1
N. brasiliensis (148)	0.5/9.6	0.5/9.6	**64**	**≥128**	**16**	**≥128**	≤1	2
N. cyriacigeorgica (264)	≤0.25/4.9	0.5/9.6	**8**	**16**	**≤4**	**16**	≤1	≤1
N. farcinica (204)	1/19	2/38	**8**	**32**	**≥128**	**≥128**	≤1	2
N. nova complex (320)	0.5/9.5	1/19	≤2	≤2	**16**	**32**	≤1	≤1
N. nova[b] (246)	0.5/9.5	1/19	≤2	≤2	**8**	**32**	≤1	≤1
N. transvalensis complex (83)	2/38	**4/76**	**64**	**≥128**	**8**	**≥128**	**32**	**≥128**

[a] Values for nonsusceptible strains, based on the 2011 CLSI intermediate and resistant breakpoints (11), are in bold.
[b] MIC_{50} and MIC_{90} for the species *N. nova* are provided independently from those for the larger *N. nova* complex.

(3%), central nervous system (3%) or ocular (2%) sites, and unknown (5%) or miscellaneous (1%) sources.

Results of antimicrobial susceptibility testing were available for 1,299 isolates (59%), including 1,267 with species-level and 32 with genus-level identification (Tables 1 and 2). Overall, resistance to TMP-SMX was rare (2%; $n = 21$) except among *N. pseudobrasiliensis* isolates (31%; $n = 4$) and members of the *N. transvalensis* complex (19%; $n = 16$). The only other TMP-SMX resistance encountered in this study was in one *N. farcinica* isolate (Table 1). Average rates of nonsusceptibility (i.e., classification as resistant or intermediate) were 5% for amikacin, 44% for ceftriaxone, 51% for imipenem, and 78% for minocycline. The highest rates of resistance to amikacin were among *N. amikacinitolerans* (57%), *N. pseudobrasiliensis* (31%), and the *N. transvalensis* complex (72%). Among the more common species, nonsusceptibility to imipenem was highest for *N. abscessus* (69%), *N. brasiliensis* (99%), *N. cyriacigeorgica* (57%), *N. farcinica* (67%), *N. otitidiscaviarum* (93%), *N. pseudobrasiliensis* (100%), and the *N. transvalensis* complex (94%). Nonsusceptibility to ceftriaxone was highest for *N. brasiliensis* (51%), *N. farcinica* (97%), *N. nova* complex (53%), *N. otitidiscaviarum* (100%), and *N. pseudobrasiliensis* (100%). Significant intraspecies variability was seen with several common species (e.g., *N. abscessus* complex, *N. cyriacigeorgica*, and *N. farcinica* for imipenem; *N. brasiliensis*, *N. nova* complex, and *N. transvalensis* complex for ceftriaxone) (Table 1; also, see Fig. S1 in the supplemental material). All 1,299 *Nocardia* isolates were susceptible to linezolid. Of the isolates that could not be identified to the species level, all were susceptible to TMP-SMX, 3% were resistant to amikacin, 44% were nonsusceptible to imipenem, 31% were resistant to ceftriaxone, and 50% were nonsusceptible to minocycline. MIC_{50} and MIC_{90} values for TMP-SMX, imipenem, ceftriaxone, and amikacin are shown in Table 2 for the 7 most common species and complexes, and the distribution of MICs is shown in Fig. S1 in the supplemental material. The mode MIC was in the intermediate range for several species/drug combinations (e.g., *N. cyriacigeorgica* and *N. farcinica* for imipenem, *N. nova* complex for ceftriaxone). Overall, amoxicillin/clavulanate, ciprofloxacin, and minocycline showed the highest rates of nonsusceptibility among the isolates (Table 1).

Nocardia spp. with resistance to two or more of the most commonly used drugs (amikacin, ceftriaxone, TMP-SMX, and imipenem), i.e., multidrug-resistant (MDR) *Nocardia* spp., are shown in Table 3. Multidrug resistance was most common among *N. pseudobrasiliensis* (100% of isolates), *N. transvalensis* complex (83%), *N. farcinica* (68%), *N. puris* (57%), *N. brasiliensis* (51%), *N. aobensis* (50%), and *N. amikacinitolerans* (43%). In contrast, all isolates of these species were susceptible to at least 1 alternative drug (in addition to linezolid) (Table 1): *N. pseudobrasiliensis* ($n = 13$) to ciprofloxacin, clarithromycin, and tobramycin; *N. farcinica* ($n = 204$) to amikacin; *N. puris* ($n = 7$) to amikacin, minocycline, and tobramycin; *N. brasiliensis* ($n = 148$) to amikacin and tobramycin; *N. aobensis* ($n = 2$) to amikacin and clarithromycin; *N. amikacinitolerans* ($n = 7$) to amoxicillin-clavulanic acid and tobramycin; and all tested isolates of the *N. transvalensis* complex ($n = 41$) to moxifloxacin. No breakpoints have been determined by CLSI or EUCAST for tigecycline; however, from our data, an ECOFF value of ≤4 μg/ml was determined. Isolates identified as resistant using this cutoff (≥8 μg/ml) were *N. farcinica* ($n = 16$; 16%), *N. nova* ($n = 1$; 0.8%), *N. transvalensis* complex ($n = 1$; 2%), and *Nocardia* spp. ($n = 1$; 6%). Of the more frequently isolated species or complexes (>10 isolates), there appeared to be three distinct susceptibility profiles for tigecycline (see Fig. S2 in the supplemental material). *N. farcinica* isolates were less susceptible than *N. beijingensis*, *N. cyriacigeorgica*, *N. nova* complex, and *N. transvalensis* complex isolates, which were in turn slightly less susceptible than *N. abscessus*, *N. brasiliensis*, *N. otitidiscaviarum*, and *Nocardia* spp. The MIC distribution for the 650 isolates with available results and separate data for multidrug-resistant isolates are shown in Table 4.

DISCUSSION

The combination of trimethoprim with sulfamethoxazole is considered the cornerstone of treatment for most *Nocardia* infections (1). More recently, there has been conflicting information on the rates of *in vitro* sulfonamide resistance among *Nocardia* spp. (5, 6, 14, 15). The interpretation of *Nocardia* MICs using the broth microdilution method is challenging. A recent multicenter study identified significant interlaboratory variability for several drug/organism combinations (16). Methodological challenges (e.g., inoculum consistency, interpretation of cutoffs) and growth characteristics of *Nocardia* appear to be responsible for limited reproducibility of broth microdilution, especially for some drug-organism combinations (5, 16). Advances in identification methods and changes in taxonomy may also explain some of the differences, especially when more recent results are compared with

TABLE 3 Susceptibility profiles of commonly used antimicrobials for *Nocardia* species with multidrug resistant isolates

Organism (*n*)	Determination for:				*n*	%
	TMP-SXT	AMK	IMI	CTR		
N. abscessus complex (110)	S	S	S	S	33	30
	S	S	S	R/I	1	0.9
	S	S	R/I	S	75	68
	S	S	R/I	R/I	1	0.9
N. amikacinitolerans (7)	S	S	S	S	2	29
	S	S	R/I	S	1	14
	S	R	S	S	1	14
	S	R	S	R/I	2	29
	S	R	R/I	R/I	1	14
N. aobensis (2)	S	S	S	S	1	50
	S	S	R/I	R/I	1	50
N. brasiliensis (148)	S	S	S	S	1	0.7
	S	S	R/I	S	72	48
	S	S	R/I	R/I	75	51
N. cyriacigeorgica (264)	S	S	S	S	106	40
	S	S	S	R/I	7	3
	S	S	R/I	S	127	48
	S	S	R/I	R/I	24	9
N. farcinica (204)	S	S	S	S	6	3
	S	S	S	R/I	60	29
	S	S	R/I	R/I	137	67
	R	S	R/I	R/I	1	0.5
N. nova complex (320)	S	S	S	S	151	47
	S	S	S	R/I	165	52
	S	S	R/I	R/I	4	1
N. pseudobrasiliensis (13)	S	S	R/I	R/I	7	54
	S	R	R/I	R/I	2	15
	R	S	R/I	R/I	2	15
	R	R	R/I	R/I	2	15
N. puris (7)	S	S	S	S	1	14
	S	S	S	R/I	2	29
	S	S	R/I	R/I	4	57
N. transvalensis complex (83)	S	S	S	S	2	2
	S	S	S	R/I	1	1
	S	S	R/I	S	9	11
	S	S	R/I	R/I	8	10
	S	R	S	S	2	2
	S	R	R/I	S	28	34
	S	R	R/I	R/I	17	20
	R	S	R/I	S	1	1
	R	S	R/I	R/I	2	2
	R	R	R/I	S	10	12
	R	R	R/I	R/I	3	4

TABLE 4 Distribution of tigecycline MICs for 650 *Nocardia* isolates

Organism (*n*)[a]	No. of isolates for which the tigecycline MIC (μg/ml) was:							
	≤0.06	0.12	0.25	0.5	1	2	4	≥8
N. abscessus complex (39)	10	7	7	10	5	0	0	0
N. abscessus complex, MDR (0)								
N. amamiensis (1)	0	0	1	0	0	0	0	0
N. amikacinitolerans (5)	0	0	0	0	3	1	1	0
N. amikacinitolerans, MDR (3)	0	0	0	0	1	1	1	0
N. aobensis (2)	0	0	0	0	1	0	1	0
N. aobensis, MDR (1)	0	0	0	0	0	0	1	0
N. asteroides sensu stricto (2)	0	1	0	0	0	1	0	0
N. beijingensis complex (18)	2	2	1	4	7	1	1	0
N. blacklockiae (1)	0	0	0	0	1	0	0	0
N. brasiliensis (88)	7	36	21	18	5	1	0	0
N. brasiliensis, MDR (34)	3	9	12	6	3	1	0	0
N. cyriacigeorgica (128)	0	7	9	39	44	24	5	0
N. cyriacigeorgica, MDR (12)	0	0	2	4	3	2	1	0
N. exalbida complex (1)	0	0	0	0	1	0	0	0
N. farcinica (102)	0	2	0	2	6	18	58	16
N. farcinica, MDR (65)	0	1	0	1	4	5	40	14
N. flavorosea (1)	0	1	0	0	0	0	0	0
N. ignorata (1)	0	0	1	0	0	0	0	0
N. neocaledoniensis (1)	0	0	0	1	0	0	0	0
N. niigatensis (1)	0	0	0	0	1	0	0	0
N. nova complex (162)	4	1	11	25	41	51	28	1
N. nova complex, MDR (2)	0	0	0	0	1	1	0	0
N. nova (132)	4	1	9	22	32	38	25	1
N. nova, MDR (2)	0	0	0	0	1	1	0	0
N. otitidiscaviarum (17)	2	3	4	3	5	0	0	0
N. paucivorans (5)	0	4	0	0	1	0	0	0
N. pseudobrasiliensis (7)	0	0	0	1	2	1	3	0
N. pseudobrasiliensis, MDR (7)	0	0	0	1	2	1	3	0
N. puris (1)	0	1	0	0	0	0	0	0
N. puris, MDR (1)	0	1	0	0	0	0	0	0
N. rhamnosiphila (2)	0	0	1	1	0	0	0	0
N. takedensis (1)	0	0	0	1	0	0	0	0
N. thailandia (1)	0	0	0	1	0	0	0	0
N. transvalensis complex (41)	0	0	4	4	11	12	9	1
N. transvalensis complex, MDR (20)	0	0	0	1	4	8	6	1
N. vermiculata (1)	0	0	1	0	0	0	0	0
N. yamanashiensis (1)	0	0	0	1	0	0	0	0
Nocardia sp. (16)	2	4	2	4	3	0	0	1
Total (650)	27	69	64	115	139	111	106	19

[a] Distribution of tigecycline MICs for the species *N. nova* is provided independently from that for the larger *N. nova* complex. Multidrug-resistant (MDR) *Nocardia* spp. were defined as those with resistance to two or more of the most commonly used drugs (amikacin, ceftriaxone, TMP-SMX, and imipenem).

those of older studies. In this large analysis, 98% of isolates were susceptible to TMP-SMX, which is consistent with data from the most recent multicenter study (5) as well as previous reports (17, 18). Resistance to TMP-SMX was highest among isolates of *N. pseudobrasiliensis* and *N. transvalensis* complex, which is consistent with previous reports and therefore are unlikely to be artifactual. Thus, our results support the notion that technical differences in susceptibility testing and interpretation, rather than an increasing prevalence of TMP-SMX drug resistance, may explain the discrepancies seen across studies.

Empirical treatment for severe *Nocardia* infections often involves combinations of TMP-SMX, imipenem, amikacin, and/or ceftriaxone (1). Susceptibility to these drugs, however, varied significantly within many species in this study (Tables 2 and 4; also, see Fig. S1 in the supplemental material). The mode MIC was in the intermediate range for several common species, including *N. cyriacigeorgica* and *N. farcinica* for imipenem as well as *N. nova* complex for ceftriaxone (Table 2; also, see Fig. S1 in the supplemental material). Resistance to two commonly used drugs was seen in *N. farcinica*, *N. pseudobrasiliensis*, and the *N. transvalensis* complex. Nonsusceptibility to three or all four drugs was present in *N. amikacinitolerans*, *N. farcinica*, the *N. transvalensis* complex, and *N. pseudobrasiliensis* isolates, resulting in infections that may be unlikely to respond to standard empirical therapies and are

more difficult to treat. Although no standardized susceptibility breakpoints exist for tigecycline, using a calculated epidemiological cutoff of ≤4 μg/ml suggests that of the more commonly isolated multidrug-resistant species, *N. farcinica* and *N. transvalensis* complex isolates are less likely to respond to this agent than MDR isolates of *N. brasiliensis* or *N. cyriacigeorgica* (Table 4). In contrast, all of the isolates tested during the study period were susceptible to linezolid. Thus, empirical treatment for severe infections due to frequently multidrug-resistant species may warrant tailored combination antimicrobial therapy in advance of more comprehensive drug susceptibility test results. These combinations could include linezolid as well as ciprofloxacin for *N. pseudobrasiliensis* and moxifloxacin for *N. transvalensis* complex (Table 1).

For patients with sulfonamide intolerance or allergy and nonserious (e.g., cutaneous) infections, several oral alternative therapies exist, including amoxicillin-clavulanic acid, minocycline, clarithromycin, and fluoroquinolones (1). The species most frequently isolated from subcutaneous/cutaneous sources in this study was *N. brasiliensis* (42%). All of these isolates were susceptible to TMP-SMX, and despite its frequent resistance to imipenem and ceftriaxone, 95% were susceptible to amoxicillin-clavulanic acid. Other species frequently isolated from subcutaneous/cutaneous sites were *N. farcinica* (13%), *N. nova* complex (9%), *N. cyriacigeorgica* (8%), and *N. abscessus* complex (5%). Susceptibility of oral regimens was highest with *N. farcinica* for amoxicillin-clavulanic acid (76%), *N. nova* complex for clarithromycin (97%), and *N. abscessus* complex for minocycline (85%) and amoxicillin-clavulanic acid (78%).

Of the 12 species first described during the period of this study, susceptibility results were available for all but *N. iowensis*. Those for which limited or no antimicrobial susceptibility data were previously available include *N. amamiensis*, *N. exalbida*, *N. niwae*, and *N. rhamnosiphila* (18, 19). All isolates of these species were susceptible to ceftriaxone. *N. niwae* isolates were susceptible to imipenem, while susceptibility varied for the other 3 species, and all but one isolate of these 4 species were resistant to amoxicillin-clavulanic acid. Interestingly, 3 of the 7 isolates belonging to the recently described species *N. amikacinitolerans* were not resistant to amikacin as has been previously reported (20). However, all 7 isolates of this species were susceptible to amoxicillin-clavulanic acid.

Given the increasingly rapid identification of *Nocardia* spp. using proteomic methods (21), the time interval between isolate identification and availability of susceptibility results will increase. We have shown that susceptibility profiles can be predicted for several of the most commonly isolated and some of the recently described *Nocardia* spp. Thus, studies such as ours begin to allow reliable prediction of antimicrobial susceptibility profiles following rapid species-level identification in many instances. Susceptibility testing should still be considered for species with variable antimicrobial susceptibility profiles or for less well characterized species, when combination therapy is warranted, and in patients with TMP-SMX intolerance.

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