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In Vitro Susceptibilities of Gram-Negative Bacteria Isolated from Hospitalized Patients in Four European Countries, Canada, and the United States in 2000-2001 to Expanded-Spectrum Cephalosporins and Comparator Antimicrobials: Implications for Therapy

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Access to current antimicrobial agent surveillance data is an important prerequisite for the optimal management of patients with hospital-acquired infections. The present study used data collected in 2000 to 2001 from 670 laboratories in Europe (France, Germany, Italy, and Spain), Canada, and the United States to report on the in vitro activities of ceftriaxone, cefotaxime, and comparative agents against >125,000 isolates of gram-negative bacteria from hospitalized patients. All but two isolates of *Enterobacteriaceae* (one isolate of *Proteus mirabilis* from France and one isolate of *Morganella morganii* from Canada) were susceptible to imipenem. The susceptibility of *Escherichia coli* to ceftriaxone or cefotaxime was ≥97% in each country, and for *P. mirabilis*, susceptibility was 99% in each country except Italy. In contrast, susceptibility of *E. coli* to ciprofloxacin varied from 80.5% (Spain) to 94.0% (France); levofloxacin susceptibility ranged from 75.2% (Spain) to 91.6% (United States). Among *Klebsiella pneumoniae* and *Klebsiella oxytoca* isolates, ceftriaxone and cefotaxime susceptibilities ranged from 86.6 to 98.7% and 83.5 to 99.7%, respectively, depending upon the country. Considerable geographic variation in the susceptibilities (generally 85 to 95% susceptible) of *Serratia marcescens* and *M. morganii* to ceftriaxone and cefotaxime were observed. For *S. marcescens*, susceptibility to piperacillin-tazobactam varied from 81.5% (France) to 94.1% (Italy) and susceptibility to ciprofloxacin ranged from 66.2% (Germany) to 90.7% (Spain). *Enterobacter cloacae* and *Enterobacter aerogenes* were less susceptible to ceftriaxone and cefotaxime than were the other species of *Enterobacteriaceae* studied. The present study demonstrated that established parenteral expanded-spectrum cephalosporin antimicrobial agents retain significant in vitro activity against many clinically important gram-negative pathogens.

Gram-negative bacteria remain important hospital pathogens, particularly for critically ill patients, and appropriate antimicrobial treatment is often critical to decreasing morbidity and mortality among hospitalized patients with infections (3, 8). Given the propensity for resistance to develop to all available antimicrobial agents, the publication of current antimicrobial susceptibility data are important, particularly for agents or classes of agents that have been frequently used clinically for prolonged periods of time and upon which physicians constantly depend. Expanded-spectrum cephalosporins such as ceftriaxone and cefotaxime are broad-spectrum agents that have been widely prescribed by physicians in Europe, Canada, and the United States for hospitalized patients with a variety of infections for almost 20 years. The intent of the present study was to provide an update on the in vitro activity of expanded-spectrum cephalosporins and comparator antimicrobial agents against gram-negative bacteria from hospitalized patients in France, Germany, Italy, Spain, Canada, and the United States by using The Surveillance Network (TSN) databases (Focus Technologies, Herndon, Va.). The implications of recent surveillance data for the therapy of hospital-acquired infections are discussed.

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MATERIALS AND METHODS

In 2000 to 2001, TSN databases assimilated antimicrobial susceptibility testing and patient demographic data from networks of hospitals in several countries, including France ($n = 63$), Germany ($n = 168$), Italy ($n = 48$), Spain ($n = 21$), Canada ($n = 87$), and the United States ($n = 283$), and these were used as the data source for this study (17). Laboratories contributing to TSN databases are all nationally accredited and are invited to participate in TSN based on factors such as hospital type (university teaching hospital or community hospital) and antimicrobial susceptibility testing method used as well as the bed size, patient population, and geographic location of the hospital(s) they serve (17). All isolates reported in TSN were identified at the participating institutions by routine methods in use at each laboratory. Antimicrobial susceptibility testing of patient isolates is conducted onsite by each participating laboratory as a part of its routine diagnostic testing. Only data generated by using nationally approved (Food and Drug Administration-approved in the United States) testing methods with MIC results interpreted according to NCCLS (Germany, Italy, Spain, Canada, and United States) (13) and SFM (Société Francaise de Microbiologie; France) recommendations (18) were included in the datasets analyzed in this study. Antimicrobial agent susceptibility data from Germany and Spain that were interpreted by breakpoints other than those of the NCCLS were excluded from the datasets analyzed; all data in TSN from Italy, Canada, and the United States were interpreted by using NCCLS breakpoints. In addition, a series of quality-control filters (proprietary critical rule sets) were used to screen susceptibility test results for patterns indicative of testing error; suspect results are removed from analysis for laboratory confirmation (17). In TSN, any result from the same patient with the same organism identification and the same susceptibility pattern received within 5 days is considered a repeat culture and is counted only once in the database.

In the present study, TSN results from 1 January 2000 to 31 December 2001 were used to determine the rates of antimicrobial susceptibility for 15 antimicrobial agents among prevalent gram-negative species isolated from hospitalized patients in Europe, Canada, and the United States. Data from patients identified as nursing home residents and hospital outpatients in hospital laboratory information systems were excluded from the analysis. An inpatient isolate was defined as such by each hospital participating in TSN. The TSN database presumes the evidence of infection, but no clinical correlates are applied universally. Thus, the data for gram-negative bloodstream and urine cultures are much more likely to reflect infection causally than the data for isolates from wounds and sputum cultures. Nevertheless, the data from microbiology laboratories are often used to guide therapy in hospital-associated pneumonia and often in skin and soft tissue infections. Overall data from all specimen sources were analyzed, as were susceptibility rates among organisms commonly isolated from patients with specific infection types. Isolate results were reported only for bacterial species-antimicrobial agent combinations in which 50 or more results were available for a specific specimen source in a country. In TSN, all isolates are not tested against all agents and variation can be observed for antimicrobial agents of the same class such as expanded-spectrum cephalosporins (ceftriaxone and cefotaxime) and fluoroquinolones (ciprofloxacin and levofloxacin) for which similar in vitro activities have been previously demonstrated.

RESULTS

The cumulative 2000 to 2001 antimicrobial susceptibilities of eight species of *Enterobacteriaceae* and *Haemophilus influenzae* from hospitalized patients are shown (Table 1). Data from both intensive-care unit (ICU) and non-ICU hospital inpatients are combined. All members of the family *Enterobacteriaceae* were susceptible to imipenem except for one isolate of *Proteus mirabilis* from France and one isolate of *Morganella morganii* from Canada. Susceptibility to amikacin exceeded 98% for the majority of species of *Enterobacteriaceae* in each country studied, and generally, susceptibility to gentamicin was >90%. *Escherichia coli* susceptibility to ceftriaxone or cefotaxime was 97% or greater in each country studied. In contrast, susceptibility to amoxicillin-clavulanate varied from 69.9% (France) to 85.8% (Spain), susceptibility to ciprofloxacin varied from 80.5% (Spain) to 94.0% (France), and susceptibility to levofloxacin varied from 75.2% (Spain) to 91.6% (United States).

Ninety-nine percent of *P. mirabilis* isolates from each country except Italy (81.0% and 71.9%, respectively) were susceptible to ceftriaxone or cefotaxime. For *Klebsiella pneumoniae* and *Klebsiella oxytoca*, ceftriaxone or cefotaxime susceptibilities ranged from 86.6 to 98.7% and 83.5 to 99.7%, respectively, depending upon the country. Considerable variation in the susceptibilities to ceftriaxone and cefotaxime of *Serratia marcescens* and *M. morganii* were also noted for isolates tested within the same country and among countries, but generally, 85 to 95% of isolates of both species were susceptible to ceftriaxone or cefotaxime. For *S. marcescens*, susceptibility to piperacillin-tazobactam varied from 81.5% (France) to 94.1% (Italy), and susceptibility to ciprofloxacin varied from 66.2% (Germany) to 90.7% (Spain).

Enterobacter cloacae and *Enterobacter aerogenes* were less susceptible to ceftriaxone and cefotaxime than were the other species of *Enterobacteriaceae* studied. Susceptibilities to cefepime, ceftriaxone, and cefotaxime were similar for *E. coli*, *K. pneumoniae*, *K. oxytoca*, and *P. mirabilis*. Cefepime susceptibilities were greater than those to ceftriaxone and cefotaxime for *Enterobacter* spp., *S. marcescens*, and *M. morganii*. All isolates of *H. influenzae* were susceptible to ceftriaxone, cefotaxime, and cefepime. Ceftazidime nonsusceptibility ranged from 0.9% (France) to 3.5% (Italy) for *E. coli* and from 1.6% (Canada) to 16.1% (Italy) for *K. pneumoniae*. Piperacillin-tazobactam susceptibilities exceeded 95% only for *E. coli* and *P. mirabilis* in each country. Variations in fluoroquinolone (ciprofloxacin and levofloxacin) susceptibilities were common for all species of *Enterobacteriaceae*. For example, for *E. coli*, the range of susceptibilities was from 75.2% (Spain, levofloxacin) to 94.0% (France, ciprofloxacin).

Table 2 provides antimicrobial susceptibility rates for *Enterobacteriaceae* isolated from hospitalized patients with potentially complicated urinary tract infections. Against *E. coli*, the most commonly isolated species from patients with potentially complicated urinary tract infections, ceftriaxone susceptibility ranged from 96.9% (Italy) to 99.7% (Germany) and cefotaxime susceptibility ranged from 95.4% (Italy) to 99.3% (France). Ciprofloxacin (range, 70.3 to 91.0%) and trimethoprim-sulfamethoxazole (TMP-SMX) (range, 61.7 to 82.7%) demonstrated greater regional variability against *E. coli*, and in each country studied, susceptibilities to ciprofloxacin (2.7 to 10.2% lower) and TMP-SMX (0.3 to 5.9% lower) were lower among urinary isolates than among all isolates (Table 1). Lower susceptibilities to ciprofloxacin and TMP-SMX, relative to all isolates, were also generally observed for *K. pneumoniae*, *K. oxytoca*, and *P. mirabilis*. Susceptibility rates to individual agents varied by gram-negative species, and a single country could not be demonstrated to have an overall greater or lower prevalence of susceptible isolates for all agents studied.

Table 3 summarizes the susceptibility results for bloodstream isolates. For *E. coli*, ≥97% of isolates were susceptible to ceftriaxone and cefotaxime in the four European countries studied, Canada, and the United States. Ciprofloxacin susceptibility in *E. coli* was variable, from 81.0% (Spain) to 93.9% (France), but less variable than isolates from the urinary tract (Table 2). Gentamicin susceptibility varied from 91.5% (Spain) to 96.8% (Germany). For *Klebsiella* species, 91.2 to 100% of isolates were susceptible to ceftriaxone and 90.9 to 98.1% of isolates were susceptible to cefotaxime. For *Pseudomonas aeruginosa*, an important opportunistic gram-negative pathogen, a wide range of susceptibility rates were observed geographically: amikacin (81.0 to 97.3%), cefepime (60.1 to 85.0%), ceftazidime (62.7 to 84.6%), ciprofloxacin (66.1 to 82.8%), imipenem (70.6 to 84.4%), and piperacillin-tazobactam (78.1 to 92.4%). In a few instances it seems interesting that the antimicrobial agent-pathogen pairs showed reduced susceptibilities across several antimicrobial agents. For example, in Italy the range of susceptibilities for *P. mirabilis* for all six antimicrobial agents varied from 52.6 to 78.4%, the lowest range for all the countries studied. However, for *S. marcescens*, the lowest range was seen in France, with susceptibilities from 69.9 to 90.9% across five antimicrobial agents tested.

Table 4 depicts the cumulative 2000 to 2001 data for the susceptibilities of five species of *Enterobacteriaceae*, *H. influenzae*, and *P. aeruginosa* isolated from lower respiratory tract infection specimens to antimicrobials. Generally, lower respiratory tract isolates of *E. coli* were 1 to 5% less susceptible than were all isolates combined to expanded-spectrum cephalosporins, ciprofloxacin, gentamicin, and TMP-SMX (Table 1): the same trend was not observed among *Klebsiella* spp., *Enterobacter* spp., and *S. marcescens.* Isolates of *P. aeruginosa* isolated

TABLE 1. Susceptibilities of nine species of gram-negative bacteria isolated from hospitalized patients in four European countries, Canada, and the United States to antimicrobials[a]

Organism	Antimicrobial agent	France		Germany		Italy		Spain		Canada		United States	
		No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible
E. coli	Amikacin	75,385	99.4	25,704	99.8	22,884	99.2	17,232	99.8	18,024	99.6	74,220	99.5
	Amoxicillin-clavulanate	83,690	69.9	6,205	78.8	21,667	80.6	24,101	85.8	19,286	79.6	45,434	81.2
	Ampicillin	33,822	53.6	21,339	58.3	23,263	56.5	19,705	39.2	52,354	64.6	135,321	57.9
	Cefepime	30,427	99.6	16,758	99.2	8,955	99.2	12,137	98.4	1,636	99.3	54,041	99.1
	Cefotaxime	82,657	99.6	44,149	99.1	19,542	97.1	22,991	98.2	18,927	97.0	54,268	98.3
	Cefpirome	14,045	99.6	NA[b]	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Ceftazidime	77,457	99.1	22,800	98.9	23,216	96.5	21,303	98.1	39,585	98.7	81,300	97.0
	Ceftriaxone	7,278	99.5	3,193	99.8	10,410	96.7	793	97.4	36,293	98.6	97,940	98.5
	Cefuroxime	11,384	92.8	35,157	91.9	7,643	87.0	14,507	91.9	20,340	92.9	54,084	91.7
	Ciprofloxacin	64,199	94.0	36,898	88.4	24,201	84.7	23,473	80.5	45,854	93.2	110,811	92.4
	Gentamicin	84,261	96.7	41,428	95.2	26,319	92.8	23,967	91.1	46,778	94.8	135,528	95.0
	Imipenem	75,852	100	37,172	100	20,230	100	13,254	100	32,838	100	87,433	100
	Levofloxacin	NA	NA	16,582	89.8	2,269	85.2	169	75.2	5,974	90.3	100,223	91.6
	Piperacillin-tazobactam	52,063	97.0	42,439	96.5	12,857	96.8	10,674	96.5	37,473	96.6	70,784	95.3
	TMP-SMX	82,535	78.6	42,715	73.2	25,640	74.4	24,379	67.6	52,224	83.5	135,210	80.7
K. pneumoniae	Amikacin	7,704	96.9	5,915	99.3	4,888	94.2	2,290	98.9	5,663	99.6	28,688	98.4
	Amoxicillin-clavulanate	8,382	82.6	1,130	76.8	4,658	79.5	3,158	87.0	5,950	93.1	16,734	90.1
	Ampicillin	3,249	0.6	4,424	0.9	4,126	1.4	2,639	0.9	14,605	1.0	46,943	1.3
	Cefepime	3,409	95.8	3,925	95.1	1,629	96.6	1,710	87.0	574	98.8	23,462	96.7
	Cefotaxime	8,378	96.1	10,088	93.8	4,135	90.4	3,052	91.3	5,919	98.3	21,812	93.6
	Cefpirome	1,360	92.8	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Ceftazidime	8,105	94.4	5,299	92.4	5,204	83.9	2,823	90.9	11,573	98.4	33,261	90.9
	Ceftriaxone	476	90.6	461	98.7	2,695	86.6	119	94.1	9,902	98.7	37,426	94.5
	Cefuroxime	1,107	81.4	8,524	86.3	1,499	72.3	1,858	89.1	6,672	90.0	20,816	81.8
	Ciprofloxacin	6,889	92.7	8,722	87.2	5,339	91.6	3,032	95.5	13,276	94.8	40,605	92.1
	Gentamicin	8,396	97.2	9,631	93.7	5,393	90.1	3,177	89.1	13,837	97.5	49,694	94.1
	Imipenem	8,007	100	9,265	100	4,772	100	1,809	100	9,430	100	35,247	100
	Levofloxacin	NA	NA	4,065	93.1	588	92.0	NA	NA	2,153	94.8	37,636	92.9
	Piperacillin-tazobactam	5,626	92.9	9,893	86.2	2,387	89.7	1,362	89.3	10,959	93.9	30,227	89.5
	TMP-SMX	8,140	87.5	9,890	83.3	5,174	82.9	3,193	85.5	14,726	92.5	49,187	89.1
K. oxytoca	Amikacin	3,624	98.4	2,990	99.8	795	98.0	840	99.6	1,475	99.8	4,710	99.2
	Amoxicillin-clavulanate	3,887	82.7	444	79.1	727	83.9	1,216	84.5	1,447	90.5	2,560	83.5
	Ampicillin	1,707	0.7	2,071	3.7	882	3.5	933	2.1	3,598	0.9	7,624	1.2
	Cefepime	1,642	97.1	1,815	94.0	602	98.5	563	94.1	110	99.1	3,955	96.5
	Cefotaxime	3,879	97.6	4,979	92.7	623	95.5	1,170	96.2	1,620	96.7	3,933	93.1
	Cefpirome	748	96.4	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Ceftazidime	3,735	98.7	2,555	94.5	929	88.7	1,160	96.8	2,814	98.1	5,790	92.4
	Ceftriaxone	291	83.5	327	99.7	518	88.6	NA	NA	2,430	97.0	6,133	90.6
	Cefuroxime	506	80.6	4,186	80.4	512	75.6	624	84.1	1,791	89.1	4,080	78.6
	Ciprofloxacin	3,298	92.5	4,122	88.1	984	93.6	1,195	94.2	3,277	97.3	6,902	91.9
	Gentamicin	3,892	96.4	4,818	97.8	993	92.6	1,215	97.9	3,444	97.0	8,162	92.4
	Imipenem	3,642	100	4,562	100	837	100	615	100	2,315	100	5,932	100
	Levofloxacin	NA	NA	1,802	92.8	284	95.8	NA	NA	492	98.4	5,751	93.1
	Piperacillin-tazobactam	2,688	87.2	4,856	80.6	766	88.0	525	89.5	2,716	93.6	4,964	86.2
	TMP-SMX	3,769	92.1	4,799	88.9	919	90.4	1,218	91.5	3,637	95.7	8,015	91.0
E. cloacae	Amikacin	6,230	97.9	3,838	99.3	2,314	96.6	1,935	99.6	3,197	99.6	15,154	98.3
	Amoxicillin-clavulanate	6,410	3.4	814	5.4	2,106	4.8	2,509	1.9	2,742	4.4	7,442	3.5
	Ampicillin	2,470	2.8	3,242	9.0	1,941	7.1	1,976	4.3	6,823	1.6	22,307	2.7
	Cefepime	3,335	91.7	2,746	96.5	1,245	93.0	1,954	93.8	298	97.3	13,595	92.2
	Cefotaxime	6,463	71.3	6,777	72.8	2,145	56.8	1,866	78.8	3,254	75.7	13,373	63.8
	Cefpirome	1,241	79.5	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Ceftazidime	6,359	70.6	4,096	68.5	2,732	57.5	1,846	74.0	5,427	79.3	18,661	64.9
	Ceftriaxone	593	52.8	446	86.8	1,584	61.1	88	72.7	4,821	78.4	18,879	66.9
	Cefuroxime	790	32.2	5,553	13.3	979	24.2	1,519	26.3	3,775	40.7	11,373	32.7
	Ciprofloxacin	5,657	85.7	5,754	90.5	2,774	77.7	2,479	96.0	6,486	93.6	20,019	87.3
	Gentamicin	6,456	89.8	6,449	95.5	2,797	77.1	2,514	99.0	6,652	96.2	24,286	89.5
	Imipenem	6,273	100	6,268	100	2,569	100	1,640	100	4,660	100	19,108	100
	Levofloxacin	NA	NA	2,806	92.3	620	68.6	NA	NA	1,098	92.3	18,087	88.7
	Piperacillin-tazobactam	5,006	73.6	6,682	73.4	1,475	64.3	1,302	74.3	5,427	77.2	15,129	70.0
	TMP-SMX	6,202	90.7	6,571	93.0	2,623	86.3	2,527	95.0	6,890	93.2	23,724	86.9
E. aerogenes	Amikacin	3,751	71.8	782	99.9	1,241	89.8	503	98.6	805	99.6	6,088	98.5
	Amoxicillin-clavulanate	3,996	2.8	198	1.5	1,164	6.4	622	4.0	771	7.1	3,408	5.7
	Ampicillin	1,727	0.4	589	2.0	1,013	2.9	531	3.8	1,820	2.1	9,814	2.9
	Cefepime	2,327	85.3	499	98.0	556	94.1	519	95.6	NA	NA	5,441	95.8
	Cefotaxime	4,029	48.2	1,291	79.0	1,024	58.6	511	74.2	816	80.9	5,335	72.2
	Cefpirome	1,131	74.1	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Continued on following page

TABLE 1—*Continued*

Organism	Antimicrobial agent	France		Germany		Italy		Spain		Canada		United States	
		No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible
	Ceftazidime	4,051	31.2	705	59.9	1,362	42.3	490	67.1	1,528	83.0	7,853	68.9
	Ceftriaxone	404	32.7	103	58.3	780	52.4	NA	NA	1,310	85.3	8,138	73.4
	Cefuroxime	689	16.4	974	57.6	456	27.0	437	42.8	953	66.4	4,853	55.9
	Ciprofloxacin	3,703	34.2	1,116	91.9	1,380	62.1	605	91.1	1,744	94.3	8,655	93.4
	Gentamicin	4,028	95.3	1,178	98.3	1,382	87.6	636	96.5	1,798	99.1	10,564	95.5
	Imipenem	4,003	100	1,201	100	1,255	100	476	100	1,300	100	7,949	100
	Levofloxacin	NA	NA	568	94.9	269	57.3	NA	NA	272	92.7	7,875	94.4
	Piperacillin-tazobactam	2,995	45.5	1,277	69.5	758	59.5	377	67.4	1,480	81.4	6,333	72.8
	TMP-SMX	3,910	52.7	1,265	94.2	1,316	61.9	637	92.0	1,847	97.0	10,325	95.7
P. mirabilis	Amikacin	11,063	97.5	4,979	99.8	4,728	99.0	2,804	99.5	2,476	99.7	13,935	99.3
	Amoxicillin-clavulanate	11,920	77.9	1,157	96.7	4,457	83.8	3,906	94.8	3,240	93.9	6,978	96.5
	Ampicillin	4,608	60.5	3,876	69.6	4,200	42.6	3,214	60.9	7,070	82.2	23,265	83.5
	Cefepime	4,625	98.9	3,368	99.6	1,594	94.2	1,995	99.0	242	96.7	9,735	98.3
	Cefotaxime	11,860	99.1	8,504	99.3	4,069	71.9	3,762	99.7	2,614	99.2	10,232	99.4
	Cefpirome	1,874	97.8	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Ceftazidime	11,298	98.9	4,624	99.1	4,811	87.8	3,464	99.4	5,659	99.1	14,604	98.4
	Ceftriaxone	635	99.7	568	98.8	1,846	81.0	91	98.9	5,141	99.5	17,912	99.5
	Cefuroxime	1,488	95.2	6,893	97.6	1,358	57.2	2,264	98.1	2,800	98.0	9,246	97.2
	Ciprofloxacin	9,866	85.8	7,319	89.1	4,963	73.2	3,833	89.3	6,349	92.4	18,586	84.6
	Gentamicin	12,006	92.7	7,930	92.6	5,007	64.9	3,921	89.7	6,653	93.5	23,429	91.4
	Imipenem	9,739	99.9	7,168	100	4,197	100	2,057	100	4,661	100	15,453	100
	Levofloxacin	NA	NA	3,336	93.1	390	77.2	NA	NA	929	98.5	18,137	85.5
	Piperacillin-tazobactam	7,840	99.2	8,456	98.8	2,077	98.2	1,739	99.4	5,344	97.6	13,618	97.7
	TMP-SMX	11,595	80.7	8,040	71.8	4,854	54.9	3,952	63.7	7,061	82.0	23,319	83.6
S. marcescens	Amikacin	2,180	90.8	1,768	98.8	1,087	97.4	705	98.0	1,775	99.1	8,296	98.2
	Amoxicillin-clavulanate	2,229	2.9	447	2.7	981	2.2	908	5.7	1,661	2.9	3,757	1.6
	Ampicillin	906	2.0	1,270	7.4	858	7.0	765	8.2	3,612	11.1	12,611	5.9
	Cefepime	1,274	98.3	1,212	98.6	610	98.2	754	97.6	133	97.7	7,313	96.8
	Cefotaxime	2,252	81.0	2,827	91.2	930	85.7	736	92.1	1,782	93.5	7,194	85.5
	Cefpirome	526	97.2	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Ceftazidime	2,214	95.8	1,808	92.1	1,279	87.7	673	94.5	3,064	96.3	10,480	89.4
	Ceftriaxone	322	65.5	316	53.8	800	85.3	NA	NA	2,594	95.7	10,511	90.6
	Cefuroxime	296	1.4	2,208	0.6	453	1.8	540	1.9	1,930	1.9	6,228	0.7
	Ciprofloxacin	2,034	76.3	2,659	66.2	1,293	88.5	915	90.7	3,559	85.4	11,138	89.5
	Gentamicin	2,269	90.0	2,472	90.8	1,294	96.0	928	97.1	3,579	94.0	13,443	94.2
	Imipenem	2,194	100	2,794	100	1,252	100	614	100	2,514	100	10,591	100
	Levofloxacin	NA	NA	1,288	83.2	298	96.3	NA	NA	563	92.2	10,233	93.5
	Piperacillin-tazobactam	1,733	81.5	2,897	85.7	726	94.1	503	91.9	3,125	92.8	9,245	87.8
	TMP-SMX	2,105	80.5	2,715	83.7	1,130	87.4	930	96.0	3,671	92.8	13,192	95.5
M. morganii	Amikacin	2,975	98.8	1,061	99.6	1,098	98.7	1,041	99.6	666	99.7	3,090	99.0
	Amoxicillin-clavulanate	3,128	1.4	254	3.9	1,015	2.9	1,356	1.3	738	1.9	1,515	3.8
	Ampicillin	1,092	0.5	871	1.3	916	1.8	1,120	0.8	1,659	1.7	4,897	3.4
	Cefepime	1,452	98.1	790	96.3	367	99.2	1,071	97.7	52	100	2,555	97.5
	Cefotaxime	3,154	87.8	1,930	89.3	903	69.3	996	89.8	717	87.3	2,441	81.8
	Cefpirome	560	93.8	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Ceftazidime	3,051	85.5	1,017	86.1	1,160	76.6	975	85.4	1,318	83.5	3,559	75.7
	Ceftriaxone	220	90.5	90	95.6	558	86.9	64	96.9	1,224	96.6	3,981	91.9
	Cefuroxime	437	8.0	1,627	4.1	345	6.1	763	4.5	787	6.2	2,607	7.8
	Ciprofloxacin	2,693	88.5	1,604	90.6	1,176	80.4	1,326	82.9	1,544	91.8	4,068	78.2
	Gentamicin	3,162	93.5	1,800	93.6	1,184	83.5	1,367	84.2	1,624	93.6	4,940	84.8
	Imipenem	2,948	100	1,638	100	1,078	100	869	100	1,009	99.9	3,636	100
	Levofloxacin	NA	NA	778	93.1	130	89.2	NA	NA	237	90.3	3,799	77.6
	Piperacillin-tazobactam	2,154	94.2	1,850	94.8	531	94.9	681	95.5	1,222	95.7	3,226	93.1
	TMP-SMX	3,034	83.0	1,881	85.7	1,124	67.8	1,372	70.1	1,673	87.2	4,880	74.7
H. influenzae	Amoxicillin-clavulanate	3,612	100	2,006	100	424	100	2,327	100	401	100	1,138	99.8
	Ampicillin	790	71.3	2,293	93.5	1,041	91.1	2,400	78.8	2,901	78.6	2,857	63.0
	Cefepime	NA	NA	NA	NA	NA	NA	513	100	NA	NA	84	100
	Cefotaxime	3,183	100	2,071	100	448	100	2,308	100	810	100	1,129	100
	Ceftazidime	NA	NA	1,610	100	309	100	NA	NA	NA	NA	108	100
	Ceftriaxone	209	100	50	100	449	100	142	100	293	100	2,051	100
	Cefuroxime	737	71.4	2,052	98.8	150	95.3	1,493	98.3	1,838	99.4	2,227	96.1
	Ciprofloxacin	538	100	2,080	100	580	100	1,756	100	533	100	352	100
	Gentamicin	3,001	74.4	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Imipenem	NA	NA	1,996	100	277	100	808	100	NA	NA	194	100
	Levofloxacin	NA	NA	769	100	371	100	343	100	104	100	1,163	100
	TMP-SMX	3,327	73.4	2,024	84.5	1,037	84.4	1,987	58.1	2,345	81.0	2,756	80.9

[a] Data are cumulative for 2000 to 2001.
[b] NA, not available, <50 results were available.

TABLE 2. Susceptibilities of gram-negative bacteria isolated from hospitalized patients with potentially complicated urinary tract infections in four European countries, Canada, and the United States to antimicrobials[a]

Organism	Antimicrobial agent	France		Germany		Italy		Spain		Canada		United States	
		No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible
E. coli	Cefotaxime	9,062	99.3	5,447	98.9	3,944	95.4	1,570	97.8	4,628	96.8	9,821	98.3
	Ceftazidime	8,498	98.6	2,474	98.4	4,001	94.1	1,538	98.5	9,025	98.6	15,593	96.7
	Ceftriaxone	1,167	99.2	906	99.7	1,440	96.9	NA[b]	NA	7,593	98.2	19,590	98.2
	Ciprofloxacin	6,045	91.0	4,017	79.4	4,112	74.8	1,105	70.3	10,060	89.4	22,440	89.7
	Gentamicin	9,548	95.4	4,863	93.0	5,268	89.4	1,621	88.4	10,903	94.2	27,780	94.2
	TMP-SMX	9,450	78.0	5,357	67.4	5,275	69.4	1,667	61.7	11,433	82.7	27,890	80.4
K. pneumoniae	Cefotaxime	1,143	94.7	1,162	92.9	789	85.0	171	95.3	1,453	97.8	3,416	93.6
	Ceftazidime	1,090	92.6	559	85.7	987	77.5	169	95.3	2,725	97.7	5,512	90.3
	Ceftriaxone	NA	NA	84	98.8	240	74.2	NA	NA	2,173	98.2	6,914	94.3
	Ciprofloxacin	771	87.4	921	80.8	996	88.0	71	91.5	3,024	93.5	7,565	90.2
	Gentamicin	1,148	97.7	1,111	90.4	1,013	87.3	173	89.6	3,265	96.9	9,396	93.8
	TMP-SMX	1,141	84.9	1,151	77.8	1,015	73.8	173	83.8	3,393	90.5	9,402	87.1
K. oxytoca	Cefotaxime	624	97.3	564	87.1	50	90.0	72	94.4	322	96.9	580	93.3
	Ceftazidime	592	98.8	229	93.0	101	87.1	71	100	592	98.8	987	93.1
	Ceftriaxone	57	86.0	NA	NA	63	93.7	NA	NA	491	98.4	1,113	90.2
	Ciprofloxacin	432	88.7	439	74.7	108	88.0	55	89.1	660	95.8	1,325	87.8
	Gentamicin	638	94.7	542	95.8	108	96.3	74	97.3	710	96.8	1,559	93.1
	TMP-SMX	638	91.7	555	74.6	108	87.0	75	85.3	746	95.8	1,566	89.0
P. mirabilis	Cefotaxime	1,684	98.8	1,406	99.2	1,110	63.6	211	100	964	98.8	1,997	99.7
	Ceftazidime	1,574	99.0	713	98.9	1,322	84.1	209	99.5	1,955	99.2	2,989	98.8
	Ceftriaxone	114	100	66	98.5	280	85.0	NA	NA	1,670	99.4	4,056	99.5
	Ciprofloxacin	1,192	81.8	1,222	82.0	1,349	64.6	129	78.3	2,176	88.8	4,443	81.5
	Gentamicin	1,729	93.2	1,275	88.9	1,364	57.3	216	86.6	2,325	94.2	5,515	90.9
	TMP-SMX	1,711	78.4	1,372	64.8	1,363	45.5	221	64.3	2,401	79.1	5,531	81.6
Other *Enterobacteriaceae*	Cefotaxime	2,574	69.2	1,561	78.7	970	61.2	251	79.7	1,320	82.5	4,010	75.2
	Ceftazidime	2,495	65.9	734	75.3	1,178	58.7	253	79.4	2,649	86.0	6,415	74.0
	Ceftriaxone	294	46.3	130	88.5	297	62.3	NA	NA	2,213	86.9	7,405	77.8
	Ciprofloxacin	1,790	55.4	1,216	73.5	1,198	55.8	153	83.7	2,956	83.6	8,069	78.9
	Gentamicin	2,591	83.0	1,382	89.0	1,215	70.7	261	89.7	3,185	91.6	9,844	88.5
	TMP-SMX	2,572	73.7	1,553	80.4	1,223	68.7	265	84.9	3,294	86.0	9,848	83.4

[a] To estimate antimicrobial susceptibilities among patients with complicated urinary tract infections, isolate specimen sources were limited to invasive specimen sources (catheterized urines, suprapubic bladder aspirates, nephrostomy, cystoscopic urine aspirates, and ureter; clean-catch urine and catheter tip isolates were excluded) from ICU and non-ICU inpatients, both males and females ≥18 years of age. The "Other *Enterobacteriaceae*" category was created for complicated urinary tract infection isolates to include *Citrobacter* spp., *Enterobacter* spp., *Providencia* spp., and *Serratia* spp. Data are cumulative for 2000 to 2001.

[b] NA, not available, <50 results were available.

TABLE 3. Susceptibilities of gram-negative bacteria isolated from bloodstream specimens of hospitalized patients in four European countries, Canada, and the United States to antimicrobials[a]

Organism	Antimicrobial agent	France		Germany		Italy		Spain		Canada		United States	
		No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible
E. coli	Cefotaxime	5,265	99.5	2,620	99.6	1,113	97.8	2,175	98.5	1,170	96.8	4,905	98.1
	Ceftazidime	4,651	98.7	1,501	99.3	1,698	97.6	2,041	98.4	2,013	98.5	6,892	96.9
	Ceftriaxone	813	99.3	186	100	1,363	98.1	492	99.4	1,585	97.9	6,460	98.2
	Ciprofloxacin	4,659	93.9	2,072	89.0	1,697	81.3	2,253	81.0	2,280	93.5	7,547	90.9
	Gentamicin	5,265	96.4	2,503	96.8	1,689	91.7	2,138	91.5	2,419	94.5	9,022	94.1
	TMP-SMX	5,090	77.9	2,524	73.5	1,490	71.5	2,229	66.4	2,535	79.8	8,854	75.7
Klebsiella spp.	Cefotaxime	846	95.7	710	95.1	313	93.0	551	90.9	618	98.1	3,143	92.2
	Ceftazidime	754	96.3	400	92.5	458	87.3	528	91.1	949	98.4	4,394	89.4
	Ceftriaxone	174	94.3	58	100	364	91.2	83	95.2	709	97.7	4,114	91.9
	Ciprofloxacin	793	94.3	581	90.9	458	94.5	587	94.0	1,083	96.1	4,663	92.5
	Gentamicin	843	98.2	665	96.8	463	92.0	566	89.9	1,177	97.2	5,472	91.8
	TMP-SMX	798	90.7	675	86.8	420	85.5	586	84.6	1,215	92.0	5,333	87.2
P. mirabilis	Cefotaxime	337	98.8	210	99.5	111	56.8	196	100	52	100	598	99.5
	Ceftazidime	297	98.3	131	99.2	171	78.4	182	100	112	100	807	98.1
	Ceftriaxone	NA[b]	NA	NA	NA	158	69.6	NA	NA	100	100	772	99.7
	Ciprofloxacin	298	85.2	174	87.4	174	63.8	206	86.9	134	95.5	849	80.0
	Gentamicin	336	93.5	198	90.9	175	52.6	197	90.4	149	92.0	1,044	87.0
	TMP-SMX	325	83.7	199	66.8	166	54.2	202	62.4	153	89.5	1,033	77.5
S. marcescens	Cefotaxime	166	76.5	162	84.0	110	89.1	90	92.2	92	88.0	759	86.0
	Ceftazidime	153	90.9	114	92.1	158	90.5	76	93.4	185	91.9	1,052	90.1
	Ceftriaxone	NA	NA	NA	NA	119	81.5	NA	NA	157	94.9	992	91.8
	Ciprofloxacin	156	69.9	155	72.9	158	93.0	98	92.9	215	93.5	1,081	92.1
	Gentamicin	167	88.6	114	88.6	159	96.9	95	100	223	91.5	1,256	94.8
	TMP-SMX	160	80.0	157	90.5	139	90.7	99	99.0	222	95.5	1,210	96.6
Citrobacter spp.	Cefotaxime	132	81.1	107	85.1	57	77.2	56	83.9	67	80.6	403	79.9
	Ceftazidime	123	79.7	66	72.7	78	68.0	51	72.6	93	82.8	554	75.6
	Ceftriaxone	NA	NA	NA	NA	60	75.0	NA	NA	64	85.9	516	80.0
	Ciprofloxacin	123	90.2	78	93.6	77	90.9	68	89.7	116	92.2	592	89.4
	Gentamicin	132	92.4	105	95.2	78	94.9	67	100	116	88.8	683	90.8
	TMP-SMX	124	89.5	110	94.6	71	90.1	68	91.2	121	87.6	663	85.7
Enterobacter spp.	Cefotaxime	658	72.5	384	78.7	290	56.9	257	70.0	322	73.0	470	72.3
	Ceftazidime	616	69.3	237	69.6	419	52.3	251	66.5	519	79.8	653	66.5
	Ceftriaxone	158	62.7	NA	NA	317	53.3	NA	NA	432	78.9	616	69.6
	Ciprofloxacin	601	79.7	312	94.9	423	72.3	323	94.4	615	96.1	669	91.8
	Gentamicin	652	95.3	354	96.9	421	80.3	305	99.7	612	96.6	795	93.7
	TMP-SMX	621	84.5	379	97.1	389	78.7	321	92.2	628	95.1	771	92.7
P. aeruginosa	Amikacin	709	81.0	176	94.9	644	84.9	446	97.3	282	90.4	2,480	92.4
	Cefepime	635	66.8	206	85.0	436	60.1	401	79.6	NA	NA	2,429	80.6
	Cefotaxime	NA	NA	139	13.0	442	9.1	325	7.4	177	21.5	1,416	9.3
	Ceftazidime	705	80.0	293	84.6	783	62.7	492	82.1	532	80.8	3,167	80.8
	Ceftriaxone	NA	NA	NA	NA	503	9.0	NA	NA	311	10.0	1,823	12.8
	Ciprofloxacin	703	67.0	262	75.2	773	66.1	487	82.8	538	78.1	3,068	73.1
	Gentamicin	700	51.6	254	79.9	775	59.5	473	75.3	505	78.6	3,448	78.7
	Imipenem	711	81.7	265	84.2	761	70.6	427	82.9	390	84.4	2,988	83.6
	Piperacillin-tazobactam	670	78.1	275	92.4	446	81.2	407	86.7	411	88.8	2,495	90.1

[a] Data are cumulative for 2000 to 2001.
[b] NA, not available, <50 results were available.

from the respiratory tract were less susceptible than *P. aeruginosa* isolates from the bloodstream in each country studied (Table 3) to amikacin (0.4 to 12.9% less), ceftazidime (3.3 to 9.3% less), ciprofloxacin (8.3 to 15.1% less), gentamicin (6.2 to 11.6% less), imipenem (6.8 to 13.4% less), and piperacillin-tazobactam (0.1 to 6.8% less). Cefepime susceptibilities were also lower (8.4 to 12.3%) for *P. aeruginosa* isolates from the respiratory tract than those from the bloodstream for each country (with data) except Italy, where susceptibilities were slightly lower (1.1%) among bloodstream isolates.

Antimicrobial susceptibilities of gram-negative bacteria isolated from skin and soft tissue specimens are summarized in Table 5 and were similar to the results reported for all isolates (Table 1). In general, isolates of *P. aeruginosa* isolated from skin and soft tissue specimens were more susceptible to amikacin, cefepime, and imipenem than isolates from the bloodstream (Table 3).

Table 6 presents antimicrobial susceptibilities of *E. coli* and *K. pneumoniae* isolated from patients in ICUs. From 93.7% (Italy) to 99.7% (Germany) of *E. coli* isolates were susceptible to ceftriaxone, and from 94.5% (Italy) to 99.0% (France) of *E. coli* isolates were susceptible to cefotaxime. For *K. pneumoniae*, from 79.4% (Italy) to 98.2% (Germany) of isolates were susceptible to ceftriaxone and 80.1% (Italy) to 98.4%

TABLE 4. Susceptibilities of gram-negative bacteria isolated from lower respiratory tract specimens of hospitalized patients in four European countries, Canada, and the United States to antimicrobials[a]

Organism	Antimicrobial agent	France		Germany		Italy		Spain		Canada		United States	
		No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible
E. coli	Cefotaxime	2,416	99.6	2,631	98.0	685	94.0	815	96.7	1,033	95.5	3,249	95.8
	Ceftazidime	2,555	98.4	1,508	97.9	899	93.1	737	97.3	1,418	97.0	4,716	93.8
	Ceftriaxone	134	97.8	213	100	674	92.6	NA[b]	NA	1,381	96.8	4,600	96.2
	Ciprofloxacin	2,300	93.6	2,200	83.8	934	90.9	841	84.7	1,719	91.2	5,042	88.0
	Gentamicin	2,422	96.2	2,548	92.9	931	94.4	836	92.1	1,974	94.0	6,218	90.6
	TMP-SMX	2,212	77.0	2,489	73.8	893	79.2	836	72.0	2,005	83.6	6,012	77.3
Klebsiella spp.	Cefotaxime	1,160	96.5	3,615	92.7	901	90.0	617	93.0	1,367	97.6	6,506	92.3
	Ceftazidime	1,287	94.7	2,065	92.0	1,103	80.3	562	94.3	1,975	98.0	9,459	89.9
	Ceftriaxone	89	91.0	180	100	904	86.7	NA	NA	1,777	98.0	9,382	92.3
	Ciprofloxacin	1,223	92.6	3,164	87.0	1,134	95.2	629	96.5	2,324	94.2	10,198	90.5
	Gentamicin	1,157	97.2	3,562	93.8	1,169	89.4	629	93.0	2,568	97.6	12,426	92.3
	TMP-SMX	1,048	90.6	3,532	85.7	1,122	88.6	631	88.6	2,625	96.0	12,011	90.6
Citrobacter spp.	Cefotaxime	350	77.7	657	81.6	136	87.5	106	88.7	208	78.9	1,024	78.6
	Ceftazidime	361	74.0	403	76.7	165	81.8	95	83.2	280	80.4	1,566	72.2
	Ceftriaxone	NA	NA	NA	NA	131	88.6	NA	NA	251	82.9	1,509	75.6
	Ciprofloxacin	336	81.6	514	90.3	169	95.3	125	91.2	338	90.8	1,591	88.1
	Gentamicin	350	89.7	651	96.5	176	98.9	125	97.6	369	88.9	1,956	91.3
	TMP-SMX	321	85.4	641	96.1	163	92.6	125	93.6	379	87.3	1,891	89.6
Enterobacter spp.	Cefotaxime	1,806	58.1	2,190	70.8	779	63.5	581	78.0	1,126	79.8	2,413	73.1
	Ceftazidime	1,926	49.7	1,421	63.4	979	57.6	579	71.7	1,602	81.8	3,471	70.7
	Ceftriaxone	180	40.0	151	74.2	731	64.8	NA	NA	1,467	81.1	3,314	73.7
	Ciprofloxacin	1,855	59.2	1,920	89.6	988	77.6	689	98.3	1,949	94.3	3,615	93.4
	Gentamicin	1,797	94.3	2,213	95.1	1,000	85.7	686	98.7	2,082	96.3	4,394	95.7
	TMP-SMX	1,681	71.7	2,140	94.1	955	81.7	688	95.6	2,127	94.9	4,194	96.1
S. marcescens	Cefotaxime	806	81.5	1,041	94.5	352	83.8	265	94.3	791	95.2	3,531	85.4
	Ceftazidime	808	95.7	728	90.1	492	85.4	239	95.8	1,205	97.2	5,254	88.6
	Ceftriaxone	128	68.0	168	51.2	331	88.2	NA	NA	994	96.1	5,104	89.4
	Ciprofloxacin	792	77.7	1,031	61.7	498	88.4	307	93.2	1,436	86.7	5,406	90.2
	Gentamicin	809	90.7	1,003	91.7	495	96.8	307	96.1	1,447	93.6	6,510	93.2
	TMP-SMX	706	79.6	977	85.8	429	87.0	307	97.7	1,461	93.0	6,352	95.7
H. influenzae	Cefotaxime	2,381	100	1,124	100	336	100	1,776	100	421	100	774	100
	Ceftazidime	NA	NA	837	100	224	100	NA	NA	NA	NA	75	100
	Ceftriaxone	159	100	NA	NA	334	100	124	100	216	100	1,578	100
	Ciprofloxacin	389	100	1,032	100	411	100	1,524	100	420	100	243	100
	Gentamicin	2,230	74.2	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	TMP-SMX	2,492	74.4	1,100	84.7	633	86.3	1,617	60.4	1,736	79.8	2,138	81.0
P. aeruginosa	Amikacin	9,072	68.1	2,632	91.7	4,729	80.8	2,857	96.9	4,479	81.2	26,459	85.8
	Cefepime	8,534	54.5	3,660	76.6	2,737	61.2	2,991	70.1	805	64.5	24,118	70.7
	Cefotaxime	NA	NA	2,402	5.5	3,538	8.7	1,768	12.7	1,789	25.0	12,781	12.3
	Ceftazidime	9,031	70.9	4,873	79.8	5,700	59.4	3,178	73.4	7,666	74.7	32,069	71.5
	Ceftriaxone	NA	NA	88	22.7	3,165	8.8	154	57.1	3,377	16.3	16,504	16.0
	Ciprofloxacin	9,057	57.3	4,737	66.0	5,405	57.8	3,182	71.2	7,529	63.0	32,012	61.0
	Gentamicin	7,993	42.4	4,581	72.1	5,571	53.3	3,163	65.8	7,516	67.0	35,769	67.1
	Imipenem	9,076	69.8	4,435	70.8	5,418	63.1	3,039	71.4	5,416	77.6	30,949	74.0
	Piperacillin-tazobactam	8,598	71.3	4,624	88.9	2,916	81.9	2,926	80.2	5,127	88.7	25,157	84.9

[a] Lower respiratory tract isolates included those from sputum, bronchial washings, and tracheal aspirates. Data are cumulative for 2000 to 2001.
[b] NA, not available, <50 results were available.

(Canada) of isolates were susceptible to cefotaxime. Differences in susceptibilities relative to all isolates were greatest for expanded-spectrum cephalosporins (up to 10% lower susceptibility among isolates from ICUs) and gentamicin (9.5%) for *K. pneumoniae*. Differences in susceptibility for isolates of *E. coli* from ICU patients relative to all isolates combined were variable and did not demonstrate an observable trend.

DISCUSSION

The goal of antimicrobial chemotherapy is to facilitate the eradication of infecting organisms from patients in a timely and safe manner while minimizing the emergence and spread of resistance. Best outcomes occur clinically if patients are given empirical therapy to which the organism is susceptible on the day infection is suspected clinically (8, 11). Our data indicate that susceptibility to ceftriaxone, piperacillin-tazobactam, imipenem, and aminoglycosides have remained relatively stable among most species of *Enterobacteriaceae* from 1996 to 2001 in the United States (10) (Table 1). The potency of ceftriaxone and cefotaxime against *E. coli* and *Klebsiella* suggests that single-agent therapy directed against those bacteria may be successful even in severely compromised hosts (25). However, the recent emergence of extended-spectrum β-lactamases and stably derepressed mutants that hyperproduce

TABLE 5. Susceptibilities of gram-negative bacteria isolated from skin and soft tissue specimens of hospitalized patients in four European countries, Canada, and the United States to antimicrobials[a]

Organism	Antimicrobial agent	France		Germany		Italy		Spain		Canada		United States	
		No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible
E. coli	Cefotaxime	4,460	99.5	2,827	99.4	638	92.6	2,964	96.1	868	96.3	1,626	96.9
	Ceftazidime	3,944	98.6	1,387	99.4	968	93.1	2,756	95.7	1,129	96.8	2,650	95.9
	Ceftriaxone	273	98.2	179	100	738	92.7	51	98.0	998	97.1	2,795	97.8
	Ciprofloxacin	3,759	92.8	2,485	92.8	1,025	82.1	3,084	77.1	1,373	91.6	3,004	90.6
	Gentamicin	4,459	94.9	2,771	96.1	1,022	88.2	3,079	86.1	1,492	92.8	3,712	93.4
	TMP-SMX	4,162	75.6	2,709	78.9	906	69.9	3,088	64.1	1,548	84.9	3,669	80.7
Klebsiella spp.	Cefotaxime	1,225	96.4	90	95.7	200	88.0	790	86.1	416	98.3	913	93.8
	Ceftazidime	1,151	95.3	437	97.3	287	82.6	752	85.5	589	97.8	1,485	90.7
	Ceftriaxone	83	88.0	54	100	216	86.6	NA[b]	NA	524	97.9	1,554	93.1
	Ciprofloxacin	1,088	94.5	764	92.5	303	90.4	825	94.9	676	93.9	1,667	90.2
	Gentamicin	1,227	97.2	895	97.4	302	91.1	822	87.5	722	97.9	2,024	94.1
	TMP-SMX	1,129	90.8	876	91.1	267	83.9	825	82.8	767	94.1	1,988	89.4
Citrobacter spp.	Cefotaxime	434	83.2	282	85.5	101	73.3	213	82.6	123	77.2	358	75.7
	Ceftazidime	403	79.7	158	71.5	144	67.4	198	81.8	146	77.4	563	74.3
	Ceftriaxone	NA	NA	NA	NA	112	69.6	NA	NA	131	71.8	561	77.7
	Ciprofloxacin	388	87.1	248	94.0	145	94.5	291	94.2	185	94.1	590	88.5
	Gentamicin	437	94.5	281	97.2	144	97.2	291	96.2	191	92.7	729	93.0
	TMP-SMX	396	89.9	271	96.3	130	95.4	291	92.1	196	89.8	717	89.4
Enterobacter spp.	Cefotaxime	1,486	71.1	494	74.7	282	64.2	630	80.2	408	72.8	195	70.8
	Ceftazidime	1,446	66.0	285	70.9	377	59.7	616	76.8	461	77.2	371	69.0
	Ceftriaxone	121	57.0	NA	NA	244	59.8	NA	NA	414	77.1	397	71.0
	Ciprofloxacin	1,386	76.9	409	91.9	379	80.0	938	94.4	595	93.6	420	95.2
	Gentamicin	1,491	93.1	493	97.8	380	85.5	938	98.2	634	98.0	489	96.1
	TMP-SMX	1,356	81.1	469	95.7	324	83.3	939	94.7	641	95.9	480	96.0
Proteus spp.	Cefotaxime	2,183	98.8	705	99.3	401	71.1	1,060	99.2	171	99.4	547	96.9
	Ceftazidime	1,963	98.8	357	98.9	505	85.0	988	98.9	249	97.6	898	98.7
	Ceftriaxone	95	99.0	95	96.8	360	75.6	NA	NA	214	99.1	1,048	96.0
	Ciprofloxacin	1,880	87.3	603	96.0	530	75.1	1,175	88.5	300	95.7	1,040	88.3
	Gentamicin	2,184	93.5	689	97.0	530	58.3	1,172	89.0	318	95.0	1,316	90.7
	TMP-SMX	1,894	81.3	659	82.9	459	54.0	1,173	66.5	332	87.7	1,296	84.6
P. aeruginosa	Amikacin	4,094	84.0	471	94.3	1,920	75.1	1,869	97.5	632	92.3	2,639	92.6
	Cefepime	3,726	71.7	580	87.8	1,227	67.7	1,915	75.3	108	80.6	2,449	80.0
	Cefotaxime	NA	NA	376	6.9	1,168	5.1	1,425	7.2	312	18.6	989	11.4
	Ceftazidime	4,090	83.8	864	89.7	2,106	61.2	2,034	77.6	1,548	85.2	3,662	79.3
	Ceftriaxone	NA	NA	NA	NA	1,305	8.4	NA	NA	606	14.2	1,852	13.2
	Ciprofloxacin	4,082	70.3	847	77.5	2,102	49.9	2,046	70.5	1,518	74.8	3,520	67.3
	Gentamicin	3,541	58.1	816	83.8	2,094	49.0	2,043	71.4	1,425	80.6	3,915	77.5
	Imipenem	4,096	83.6	844	84.6	1,931	77.2	1,929	81.0	1,159	87.8	3,393	83.4
	Piperacillin-tazobactam	3,835	83.1	775	93.9	1,161	77.3	1,846	84.5	929	92.4	2,863	88.7

[a] Skin and soft tissue infection specimen sources were skin, skin ulcer, decubitis ulcer, subcutaneous biopsy, skin biopsy, abscess, soft tissue, surgical wound, subphrenic abscess, drainage pus, splenic abscess, renal abscess, perirectal abscess, liver abscess, pancreatic abscess, and intraabdominal abscess. Data are cumulative for 2000 to 2001.

[b] NA, not available, <50 results were available.

chromosomal β-lactamases has the potential to diminish the activity of all expanded-spectrum cephalosporins against these pathogens. In the United States, the prevalence of potential extended-spectrum β-lactamase-producing isolates of *E. coli* and *K. oxytoca* (MICs of ceftazidime interpreted as intermediate and resistant) increased from 0.9 to 1.6% and from 2.9 to 5.9%, respectively, between 1996 and 2000 (10).

The present report and previous reports indicate that fluoroquinolone susceptibility appears less stable than susceptibility to other classes of antimicrobials and has decreased over time in a consistent stepwise manner for members of the family *Enterobacteriaceae*, *P. aeruginosa*, and *S. aureus* in both the United States and Europe (4, 6, 10, 12). The widespread cumulative use of fluoroquinolones (ciprofloxacin and levofloxacin) may be accelerating the development of resistance to these agents and may be the driving force behind increases in resistance (2, 12, 14, 15). Fluoroquinolone resistance among species of gram-negative bacilli appears to be found more commonly as a component of multidrug-resistant phenotypes than as a single-agent resistance phenotype (16, 24). The potential for commonly encountered gram-negative bacilli to acquire cross-resistance to several antimicrobial agents has been well documented (9, 24).

Infections of the urinary tract are the most common nosocomial infections. They account for approximately 40% of infections and are usually catheter-associated (21). Most bacteriuric episodes in patients with short-term catheterization result from a single species, primarily *E. coli*. However, *K. pneumoniae*, *P. mirabilis*, *Staphylococcus epidermidis*, enterococci, *P. aeruginosa*, and *Candida* are also common. Some clinical data have suggested that antimicrobial treatment of catheterized patients with symptomatic bacteriuria may not be

TABLE 6. Susceptibilities of gram-negative bacteria isolated from ICU patients in four European countries, Canada, and the United States to antimicrobials[a]

Organism	Antimicrobial agent	France		Germany		Italy		Spain		Canada		United States	
		No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible	No. of isolates	% Susceptible
E. coli	Cefotaxime	6,031	99.0	3,449	98.0	1,105	94.5	1,428	96.6	1,886	96.4	5,745	96.9
	Ceftazidime	5,896	98.1	1,769	98.1	1,525	94.3	1,220	97.2	2,861	97.9	9,412	95.6
	Ceftriaxone	531	98.9	353	99.7	888	93.7	NA[b]	NA	2,618	97.1	10,182	97.6
	Ciprofloxacin	5,504	93.6	2,695	87.8	1,570	89.5	1,321	81.7	3,197	90.9	11,130	90.6
	Gentamicin	6,104	95.7	2,783	94.5	1,596	93.6	1,469	90.8	4,332	94.3	13,127	92.7
	TMP-SMX	5,841	78.3	3,264	74.7	1,473	77.7	1,476	66.9	4,395	84.9	12,921	79.5
K. pneumoniae	Cefotaxime	1,034	94.2	1,505	92.0	598	80.1	496	84.9	817	98.4	4,081	91.4
	Ceftazidime	1,061	92.2	838	87.6	759	70.1	451	85.6	1,456	98.1	6,295	88.2
	Ceftriaxone	71	85.9	108	98.2	608	79.4	NA	NA	1,216	97.9	6,638	92.1
	Ciprofloxacin	977	89.1	1,331	84.6	799	91.6	475	91.2	1,595	92.4	7,150	90.4
	Gentamicin	1,031	97.9	1,274	89.6	819	81.1	514	79.6	1,857	96.8	8,481	91.4
	TMP-SMX	971	88.3	1,450	78.8	759	84.6	514	84.6	1,877	93.2	8,198	88.7

[a] Data are cumulative for 2000 to 2001.
[b] NA, not available, <50 results were available.

particularly useful in preventing complications (21). While consensus guidelines exist for the management of acute uncomplicated cystitis and pyelonephritis in otherwise healthy adult females (20), consensus guidelines are not currently published to guide the treatment of complicated urinary tract infections. In the present investigation, an average of 97% of *E. coli* in the countries studied remained susceptible to ceftriaxone and cefotaxime, suggesting that these antimicrobial agents remain an important therapeutic option for complicated urinary tract infections. *K. pneumoniae*, *K. oxytoca*, and *P. mirabilis* were also generally >90% susceptible to ceftriaxone or cefotaxime in the countries studied. Cefotaxime and ceftriaxone susceptibility was lower for these three pathogens in Italy than the other countries studied.

A recent analysis using the concept of attributable mortality (23) suggested that nosocomial bloodstream infections represent a leading cause of death in the United States (22). In the prospective surveillance system called SCOPE, nosocomial bloodstream infections caused by *E. coli*, *Klebsiella* spp., *Enterobacter* spp., *Pseudomonas* spp., and *Serratia* spp. had crude mortalities of, respectively, 24, 27, 28, 33, and 26% (5). Early initiation of appropriate antimicrobial agent treatment is critical in decreasing morbidity and mortality among patients with bloodstream infections due to gram-negative organisms (3, 8). The appropriateness of antimicrobial agent therapy should be reviewed within 24 h of the final susceptibility report becoming available from the laboratory (7). Combinations of antimicrobial agents are recommended for empirical therapy of patients with bloodstream infections, particularly for those patients with the most adverse prognostic factors (25). Clinicians need to take into account the different rates of resistance in ICUs and wards as well as the probability of *P. aeruginosa* when considering empirical therapy for infections with possible Gram-negative bacillary etiologies. Ceftriaxone, cefotaxime, and cefepime all have similar indications for pneumonia, skin and skin structure infections, and urinary tract infections; only ceftriaxone and cefotaxime have an indication for the sepsis syndrome. Our data suggest that the susceptibility of *E. coli* (>98%), *K. pneumoniae* (>91%), and *P. mirabilis* (>99%, except Italy) to ceftriaxone and cefotaxime remains high. However, ceftazidime, cefepime, imipenem, and meropenem appear most active against *P. aeruginosa* (25) (Table 3).

Pneumonia accounts for 15 to 20% of all hospital-acquired infections (19); in ICUs, pneumonia is generally the most common infection type. Hospital-acquired pneumonia accounts for the majority of deaths attributed to nosocomial infections (19), and *Enterobacteriaceae*, *P. aeruginosa*, *Streptococcus pneumoniae*, *H. influenzae*, and *Staphylococcus aureus* are the primary etiologic agents. Ceftriaxone and other nonpseudomonal expanded-spectrum cephalosporins are recommended by the American Thoracic Society for the treatment of patients with mild to moderate hospital-acquired pneumonia, provided that patients do not have risk factors which might alter the likely causative pathogens (1). Nonpseudomonal expanded-spectrum cephalosporins are also recommended for those patients with severe disease, provided that infection occurs within less than 5 days of hospital admission (1). In the present study, susceptibility data for respiratory isolates (Table 4) and isolates from patients in ICUs (Table 6) support such therapies for gram-negative bacilli under current empirical guidelines.

Skin and soft tissue infections in hospitalized patients are most commonly attributable to gram-positive bacteria (*S. aureus*, *Streptococcus pyogenes*, *Streptococcus agalactiae*). However, gram-negative bacteria, including species of *Enterobacteriaceae*, may also be etiologic agents. In addition to demonstrating almost uniform susceptibility to methicillin-susceptible *S. aureus*, *S. pyogenes*, and *S. agalactiae* (10), susceptibility to expanded-spectrum cephalosporins such as ceftriaxone and cefotaxime is high among *Enterobacteriaceae* species isolated from skin and soft tissue specimen sources (Table 5).

In conclusion, in an international study of over 125,000 isolates from 670 laboratories, our data suggest that the susceptibilities of *Enterobacteriaceae* and *P. aeruginosa* to some classes of antimicrobial agents are decreasing, most notably to the fluoroquinolones (ciprofloxacin and levofloxacin). Certain well-established antimicrobial agents, including parenteral expanded-spectrum cephalosporins, continue to retain high rates of susceptibility against many clinically important gram-negative pathogens. With respect to aminoglycosides, the susceptibility of *Enterobacteriaceae* to amikacin exceeded 98% and that

to gentamicin was over 90%. Resistance to imipenem was identified in only two isolates of *Enterobacteriaceae*.

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