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Antimicrobial Agent Susceptibility Patterns of Bacteria in Hospitals from 1971 to 1982

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Bacterial susceptibility to 16 commonly used antibiotics was analyzed for a 12-year period (from 1971 to 1982, inclusive). Susceptibilities of 5,828,243 strains isolated from a mean of 242 hospitals nationwide and of 194,575 strains isolated at the Massachusetts General Hospital, Boston, Mass., and the Bronx Lebanon Hospital Center, New York, N.Y., were compared. Strains of *Escherichia coli*, *Staphylococcus aureus*, *Haemophilus influenzae*, and *Pseudomonas aeruginosa* showed virtually the same susceptibilities to antibiotics throughout the 12-year period, whereas *Streptococcus faecalis* and *Staphylococcus epidermidis* showed significant increases in resistance to most antibiotics. The close similarity between antibiotic susceptibilities shown at both the 242 hospitals and the 2 individual hospitals suggests that this analysis accurately reflects trends of bacterial resistance to antibiotics in U.S. hospitals. Since most of the species analyzed produce serious disease and high mortality, their susceptibility to antibiotics is relevant both to physicians treating infectious diseases and to epidemiologists.

Bacterial resistance to penicillin first became evident within a few years of its introduction. Before 1946, 85% of *Staphylococcus aureus* strains were highly susceptible to penicillin; today, only 11% remain susceptible (12). The medical community has been warned repeatedly of major increases in bacterial resistance (23, 28, 34, 39, 41), with many reports citing the increased resistance of *S. aureus* to methicillin (1, 4, 5, 7, 8, 11, 19, 41, 44, 49) and gentamicin (5, 10, 11, 44, 48), of *Haemophilus influenzae* to ampicillin (16, 20, 27, 51), of gram-negative bacilli, especially *Pseudomonas aeruginosa*, to aminoglycosides (13, 17, 24, 31, 32, 37, 38, 50), and the increasing multiple drug resistance among enterococci (30, 33). The new cephalosporins appear to be responsible for bacterial cross-resistance to several beta-lactam antibiotics and occasionally to the aminoglycosides (43).

To assess the magnitude and trends of resistance to the established antibacterial agents (hereafter called antimicrobial agents) in the United States, we analyzed more than 10^7 strains of bacteria. All of these strains had been isolated from hospitals around the country during a 12-year period, and most data were filed on a nationwide computer. This computerized information was compared with that obtained additionally from two hospitals known to have accurate laboratory testing procedures and a well-balanced use of antibiotics in patients, the Massachusetts General Hospital (MGH) in Boston and the Bronx Lebanon Hospital Center (BLHC) in New York.

MATERIALS AND METHODS

We obtained data on 9,919,999 bacterial strains from Bac-Data Medical Information Systems, Inc. (Clifton N.J.), a national bacteriological monitoring service for hospital laboratories. From January 1971 to December 1982, Bac-Data collected these laboratory data from 150 to 329 (mean, 242) acute care hospitals of 100 beds or more (in 1982, of the 252 participating hospitals, 96% were accredited by the Joint Commission on Accreditation of Hospitals, and 37% were affiliated with a medical school), which were evenly dispersed throughout the country (2). These subscribing institutions report that bacterial identification was made by conventional methods and that susceptibility testing was done by disk test by the Bauer-Kirby technique (3). Only truly susceptible strains were called susceptible, whereas those with intermediary or equivocal results were labeled resistant so as not to underestimate the levels of resistance. Multiple isolates from the same patient or identical isolates from several patients were not excluded.

Of these nearly 10^7 strains, we analyzed the susceptibilities of the most frequently isolated organisms or those causing the most fatalities (a total of 5,828,243 strains) to 16 commonly used antimicrobial agents. These organisms were: *Escherichia coli*, 1,808,337 strains; *S. aureus*, 989,263 strains; *Staphylococcus epidermidis*, 688,200 strains; *P. aeruginosa*, 499,667 strains; *Streptococcus faecalis*, 563,494 strains; *Klebsiella pneumoniae*, 628,855 strains; *Proteus mirabilis*, 504,291 strains; and *H. influenzae*, 146,136 strains.

We also obtained susceptibility results for the most frequently isolated organisms at MGH over the 10-year period from 1971 to 1981 (six species totaling 171,610 strains), as reported yearly in the MGH laboratory newsletter (A. H. Goroll and A. G. Mulley, ed.), and at BLHC over the 5-year period from 1978 to 1982 (six species totaling 22,965 strains). These data were compared to the nationwide susceptibility results obtained from Bac-Data.

RESULTS

From 1971 to 1982, *E. coli* accounted for 19.2% of all Bac-Data isolated species, immediately followed by *S. aureus* at 10.5% and *S. faecalis* at 6.3%. None of these organisms showed a statistically significant increase in incidence during this 12-year period. The incidence of *S. epidermidis*, on the other hand, rose from 6.2 to 8.5%, *P. aeruginosa* rose from 7.7 to 8.4%, and *H. influenzae* rose from 0.9 to 1.8% during this time, whereas the incidence of *Klebsiella* spp. decreased from 9.1 to 6.7% and *Proteus* sp. decreased from 9.5 to 6%. These accounted for 67.4% of all organisms isolated in the 1982 Bac-Data files.

Results of the 1971 to 1982 annual surveys of the in vitro susceptibilities of these organisms to 16 antibiotics commonly used during this 12-year period are shown in Fig. 1 through 8. Included among the findings were the following.

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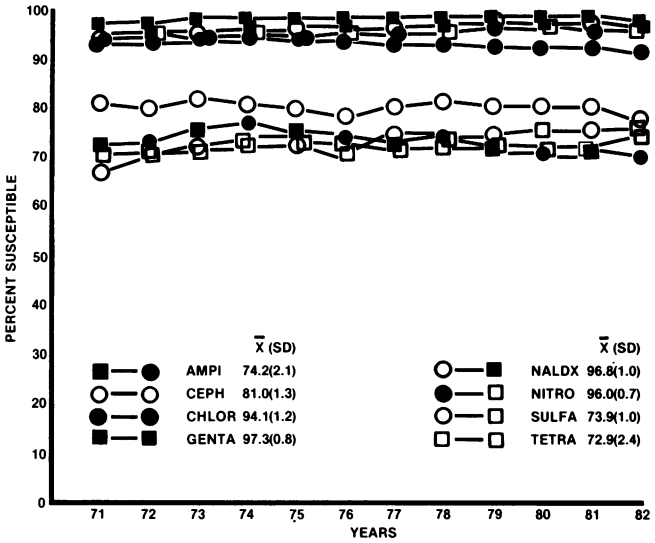

FIG. 1. Percentage of *E. coli* strains susceptible to various antibiotics. Abbreviations: AMPI, ampicillin; CEPH, cephalothin; CHLOR, chloramphenicol; GENTA, gentamicin; NALDX, nalidixic acid; NITRO, nitrofurantoin; SULFA, sulfonamides; TETRA, tetracycline; x̄, mean; SD, standard deviation.

E. coli showed no significant change in susceptibility to any of these antibiotics during the 12 years, although there were small increases in its susceptibility to tetracycline, nalidixic acid, and nitrofurantoin (Fig. 1). Likewise, *S. aureus* showed a slight increase in susceptibility to tetracycline, a slight decrease to erythromycin, and a 17% decrease in susceptibility to penicillin; its susceptibility to the other antibiotics, including oxacillin, remained stable. Except for the years 1976 and 1977 when some vancomycin-resistant strains were reported, all strains reported from 1978 to 1982 were susceptible to vancomycin (Fig. 2). *P. mirabilis* continued to remain resistant to tetracycline, and its low susceptibility to nitrofurantoin is decreasing further (Fig. 3). The

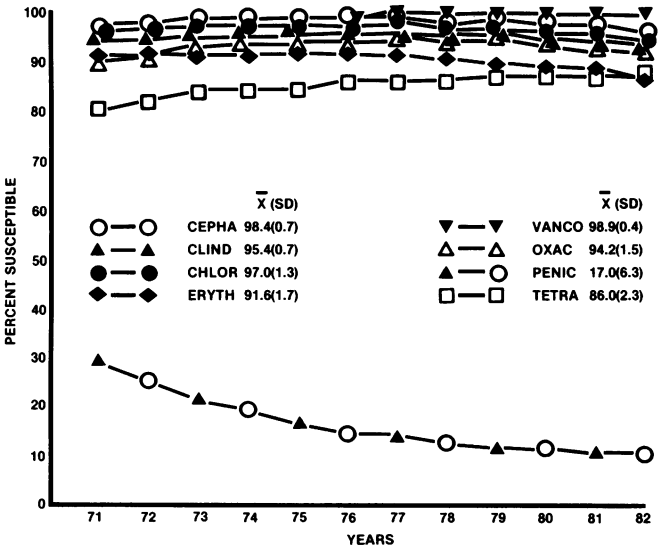

FIG. 2. Percentage of *S. aureus* strains susceptible to various antibiotics. Abbreviations: CEPHA, cephalothin; CLIND, clindamycin; CHLOR, chloramphenicol; ERYTH, erythromycin; VANCO, vancomycin; OXAC, oxacillin; PENIC, penicillin; TETRA, tetracycline; x̄, mean; SD, standard deviation.

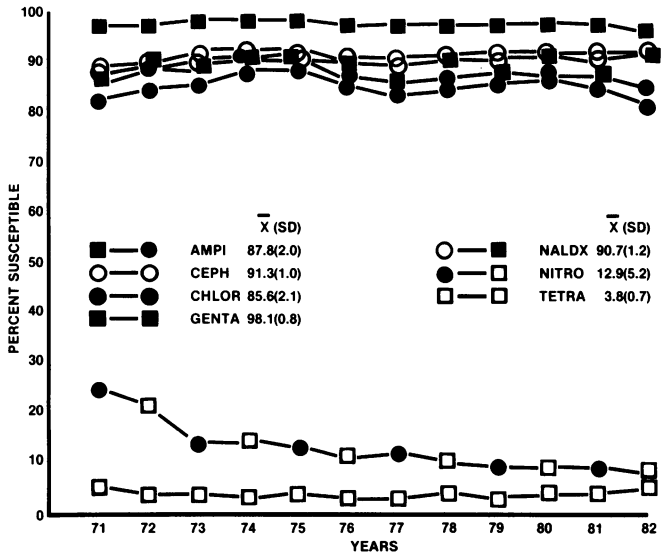

FIG. 3. Percentage of *P. mirabilis* strains susceptible to various antibiotics. For abbreviations, see the legend to Fig. 1.

susceptibility of *H. influenzae* to chloramphenicol and ampicillin remained unchanged (Fig. 4). The susceptibility of *P. aeruginosa* to carbenicillin increased, remained unchanged to colistin, and decreased to gentamicin and tobramycin (Fig. 5). *K. pneumoniae* remained resistant to ampicillin, and its susceptibility remained stable to chloramphenicol and nalidixic acid and increased to tetracycline, cephalothin, and sulfamethoxazole (Fig. 6). Its susceptibility to gentamicin decreased 7% in 1976 and has remained stable since (Fig. 6). *S. epidermidis* has shown a decrease in susceptibility to all antimicrobial agents except tetracycline (Fig. 7). *S. faecalis* showed decreases in susceptibility to cephalothin, chloramphenicol, erythromycin, and penicillin and slight increases to ampicillin, gentamicin, and nitrofurantoin (Fig. 8).

Overall, of 53 Bac-Data analyses of the antibacterial effects of different antimicrobial agents, 8 analyses showed

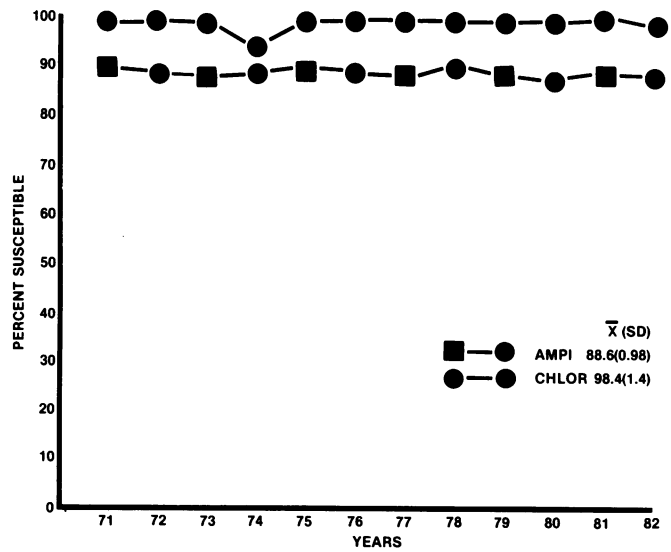

FIG. 4. Percentage of *H. influenzae* strains susceptible to various antibiotics. Abbreviations: AMPI, ampicillin; CHLOR, chloramphenicol; x̄, mean; SD, standard deviation.

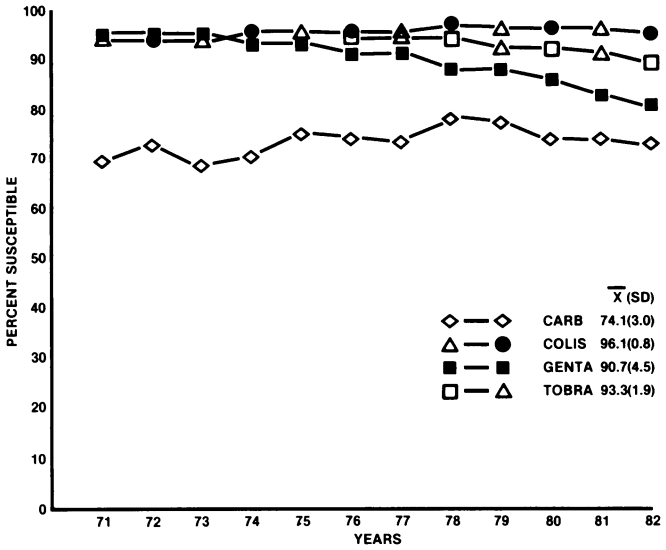

FIG. 5. Percentage of *P. aeruginosa* strains susceptible to various antibiotics. Abbreviations: CARB, carbenicillin; COLIS, colistin; GENTA, gentamicin; TOBRA, tobramycin.

increases in bacterial susceptibility, 16 showed decreases, and 29 showed virtually no change in susceptibility between 1971 and 1982. Moreover, in 25 of the 53 analyses, over 90% of strains remained highly susceptible to the drugs to which they were exposed.

Susceptibility data from MGH and BLHC are shown in Table 1 and are comparable in all respects to those obtained from Bac-Data. During the 10-year period, most species showed only minor variations in their susceptibilities to most antibiotics (notice the small standard deviations). Although MGH showed more strains of *E. coli*, *K. pneumoniae*, and *P. mirabilis* susceptible to ampicillin and carbenicillin and BLHC reported lower susceptibility for these species than Bac-Data, these differences are not statistically significant ($P > 0.5$).

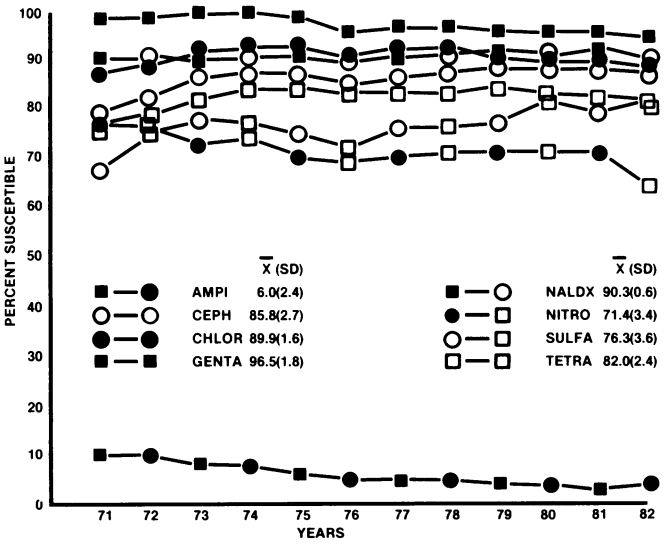

FIG. 6. Percentage of *K. pneumoniae* strains susceptible to various antibiotics. For abbreviations, see the legend to Fig. 1.

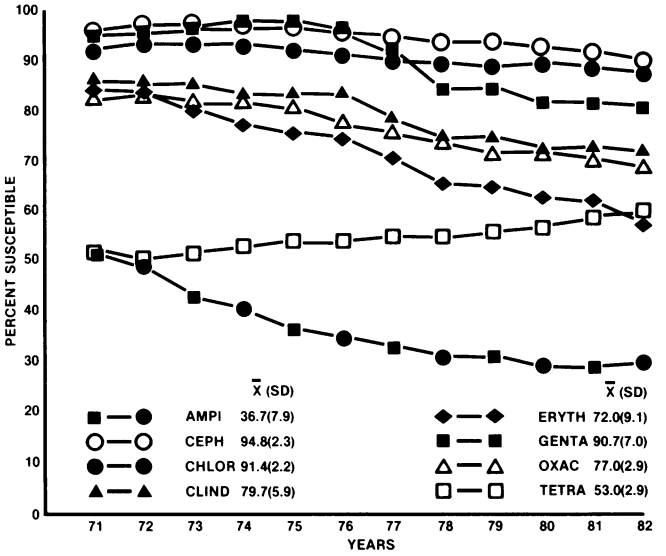

FIG. 7. Percentage of *S. epidermidis* strains susceptible to various antibiotics. Abbreviations: AMPI, ampicillin; CEPH, cephalothin; CHLOR, chloramphenicol; CLIND, clindamycin; ERYTH, erythromycin; GENTA, gentamicin; OXAC, oxacillin; TETRA, tetracycline; x̄, mean; SD, standard deviation.

DISCUSSION

The large number of strains tested against various antimicrobial agents (representing 43,246,169 individual tests) minimized possible errors incurred by individual laboratories. The College of American Pathologists showed that the accuracy in 1972 was >90%, and during 1979 to 1981 it was 95.2% (15). This is an indication that susceptibility tests performed in American hospitals, including those reporting susceptibility results to Bac-Data, show a high degree of accuracy. The close similarity between the Bac-Data susceptibility levels and trends and those from the two individual hospitals suggests that the information obtained from Bac-Data accurately represents bacterial susceptibilities to anti-

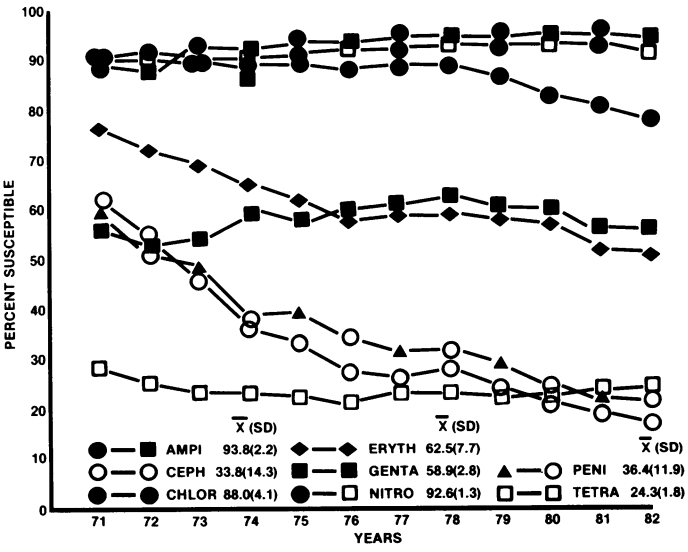

FIG. 8. Percentage of *S. faecalis* strains susceptible to various antibiotics. Abbreviations: AMPI, ampicillin; CEPH, cephalothin; CHLOR, chloramphenicol; ERYTH, erythromycin; GENTA, gentamicin; NITRO, nitrofurantoin; PENI, penicillin G; TETRA, tetracycline; x̄, mean; SD, standard deviation.

TABLE 1. Percentage of susceptible strains isolated at MGH and BLHC during the years 1971 to 1981 and 1978 to 1982, respectively

Organism and drug	Mean % of susceptible strains (SD) at following hospital:	
	MGH	BLHC
E. coli		
Ampicillin	77.3 (0.9)	67.8 (1.3)
Cephalothin	83.7 (3.7)	90.0 (1.8)
Chloramphenicol	92.4 (2.8)	94.3 (1.0)
Tetracycline	70.9 (1.5)	75.0 (3.7)
Gentamicin	98.4 (0.5)	99.5 (0.6)
Nalidixic acid	96.8 (1.0)	
Nitrofurantoin	96.0 (0.7)	97.2 (0.6)
Sulfonamides	73.9 (2.4)	71.0 (1.4)
K. pneumoniae		
Ampicillin	9.4 (2.9)	4.0 (2.5)
Cephalothin	86.0 (1.9)	93.4 (2.1)
Chloramphenicol	81.0 (2.3)	93.2 (2.2)
Tetracycline	78.5 (2.8)	89.2 (2.9)
Gentamicin	92.9 (4.7)	97.2 (0.8)
Nalidixic acid		97.2 (2.6)
Nitrofurantoin	76.0 (7.2)	88.4 (3.4)
P. mirabilis		
Ampicillin	94.7 (1.3)	86.0 (5.0)
Cephalothin	97.0 (1.6)	91.6 (3.6)
Chloramphenicol	91.9 (2.5)	91.0 (3.4)
Tetracycline		3.8 (1.6)
Gentamicin	98.4 (0.8)	99.2 (0.8)
Nalidixic acid		96.2 (2.6)
Nitrofurantoin	3.9 (2.6)	11.2 (6.1)
P. aeruginosa		
Carbenicillin	80.7 (3.5)	78.0 (3.3)
Gentamicin	87.8 (7.4)	85.4 (5.7)
Tobramycin	95.0 (3.4)	95.4 (3.3)
Colistin	98.4 (1.1)	
S. aureus		
Oxacillin	97.0 (3.3)	96.8 (1.3)
Penicillin G	15.3 (3.8)	4.5 (1.9)
Cephalothin	98.4 (1.9)	94.4 (0.9)
Erythromycin	88.7 (5.3)	91.2 (1.9)
Clindamycin	93.1 (5.7)	97.4 (1.1)
Chloramphenicol	94.9 (3.2)	97.0 (1.2)
Tetracycline	90.1 (2.3)	89.2 (6.2)
S. faecalis		
Ampicillin		95.4 (1.1)
Penicillin G	27.9 (6.0)	42.6 (24.8)
Cephalothin	20.1 (8.9)	25.6 (12.5)
Erythromycin	56.9 (13.2)	74.2 (6.2)
Chloramphenicol	77.4 (2.1)	86.8 (5.1)
Gentamicin		78.4 (9.0)
Tetracycline	19.4 (2.8)	24.0 (9.2)
Nitrofurantoin	94.9 (1.5)	

biotics in U.S. hospitals. However, it should be noted that we have included Bauer-Kirby intermediate zone sizes as resistant so as not to understate resistance prevalence. This could result in a slight overestimate of resistance in some cases, although this should not interfere with the validity of our conclusions concerning national trends. Since infections with most of the species analyzed result in serious illness with high mortality (*S. aureus* [9, 42], *E. coli* [14, 21, 29], *P. aeruginosa* [6, 46], and *S. faecalis* [25, 45]), the susceptibility data reported above are highly relevant both to physicians treating infectious diseases and to epidemiologists.

The appearance of ampicillin resistance in *H. influenzae* 1 to 3 years before the recognized identification of plasmid-borne ampicillin resistance should be discussed. The Bac-Data figures are based on Bauer-Kirby tests, and we have chosen to err on the side of resistance by including isolates showing intermediate zone sizes as resistant. Thus, the ca. 10% regarded as resistant includes isolates originally classified as intermediate. It is now recognized that ampicillin resistance in *H. influenzae* as measured by diffusion tests may yield a certain percentage of false-positive results. It is also possible that clear-cut plasmid-mediated resistance did exist before its recognition in 1974, and the frequency of reported ampicillin therapeutic failures with *H. influenzae* in the early 70s does little to dissuade us of that possibility. The levels of vancomycin resistance in *S. aureus* in 1976 and 1977 could also result from disk intermediate zones in those years that Bac-Data records were first kept for this agent. Although the 6% *Haemophilus* resistance to chloramphenicol obtained from Bac-Data in 1974 was not noted in the literature during that and the following year, three reports of chloramphenicol resistance were published during 1976 (19, 22, 26), and one appeared in 1978 (18).

It has been reported that bacterial resistance to antimicrobial agents is increasing worldwide, the United States included (35, 36). In contrast, a study conducted in Switzerland concluded that bacterial resistance to antimicrobial agents in that country has not changed during the years 1974 to 1979 (47), and one of us (2) reached the same conclusion for the years 1973 to 1977 for a large group of hospitals in the United States. Many of the resistance reports are based on surveys conducted in a single institution, in which resistance may be a consequence of unbalanced antibiotic usage or due to a high rate of nosocomial infections (1, 11, 17, 19, 31). Some reports of bacterial resistance are supported by very limited evidence; for example, one series discusses only 28 strains of *H. influenzae* resistant to ampicillin from a total of 256 strains analyzed (16, 20, 27, 51). Two of these four publications actually report a single resistant strain each (16, 27). Since 1971, 6,383 papers on bacterial resistance have been published in the English language alone. Indeed, the very abundance of literature on this subject contributes to the perception that bacterial resistance to antimicrobial agents is growing at an alarming pace. It is understandable that many of us judge antimicrobial agent profiles of bacteria by limited observations in large tertiary-type institutions of our own or of our colleagues. As one would expect, it is precisely in that setting that the selective pressure for resistance is at its peak. In addition, it is the organism with the exceptional antibiogram that remains uppermost in the minds of the observers and leads to the conclusion that antimicrobial susceptibility is undergoing dramatic changes.

Although our study confirmed that *S. faecalis* (which is naturally resistant to many antibiotics) and *S. epidermidis* (which in most cases remains a colonizing organism) have developed additional resistance to antibiotics, the other species analyzed showed little change in antimicrobial agent susceptibility during the last 12 years. Although local outbreaks of bacterial resistance do arise and many have serious consequences, bacterial susceptibility on a national scale has remained virtually unchanged during the last decade. This may, perhaps, be credited to the continuous effort in U.S. hospitals to achieve balanced usage of antibiotics.

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