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Comparison of a Highly Automated 5-h Susceptibility Testing System, the Cobas-Bact, with Two Reference Methods: Kirby-Bauer Disk Diffusion and Broth Microdilution

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The results of susceptibility tests performed with the Cobas-Bact system were compared with those of the Kirby-Bauer disk diffusion and the broth microdilution methods. The evaluation included tests with 24 antibiotics against 250 isolates of the family *Enterobacteriaceae* and 13 antibiotics against 100 gram-positive cocci. Complete agreements between the Cobas-Bact and Kirby-Bauer methods were 82.8 and 84.5% for gram-positive cocci and gram-negative bacilli, respectively. Agreements between the Cobas-Bact and broth microdilution methods were 76.7% for gram-positive cocci and 84.8% for gram-negative bacilli. Complete agreements between the Kirby-Bauer and broth microdilution methods were 87.0% for gram-positive cocci and 92.2% for gram-negative bacilli. Despite generally satisfactory results with most organism-antibiotic combinations tested, additional modifications of the Cobas-Bact system are required to reduce the number of major and very major discrepancies, as well as to permit testing of *Pseudomonas* spp. and other gram-negative nonfermentative bacilli.

In an effort to meet the demand for rapid, accurate antimicrobial susceptibility testing, a variety of automated instruments have been developed by commercial companies and evaluated in clinical microbiology laboratories (1, 2, 4–7, 9, 10, 13–17). During the last 2 years, we have had the opportunity to work with one such system, the Cobas-Bact (CB; Roche Diagnostica, Basel, Switzerland). The system is designed to perform antimicrobial susceptibility tests and microbial identifications in less than 5 h in an automated fashion. Preliminary evaluations have indicated that this system can be used for routine susceptibility tests, direct testing of positive blood culture specimens, and identification of gram-negative bacilli (3, 8). However, in a four-laboratory collaborative study, we observed some problems with susceptibility tests performed in the CB system (P. R. Murray, R. Hom, W. Martin, and G. Rypka, Abstr. Annu. Meet. Am. Soc. Microbiol. 1985, C82, p. 313). Specifically, an unacceptable level of performance was observed when ampicillin, carbenicillin, cephalothin, and nitrofurantoin were tested against gram-negative bacilli and when gentamicin, clindamycin, erythromycin, methicillin, trimethoprim-sulfamethoxazole, and vancomycin were tested against gram-positive cocci. After that preliminary report, the manufacturer modified the program software and the concentration of specific antibiotics tested in the CB system. This report summarizes the in vitro evaluation of the modified system.

MATERIALS AND METHODS

CB system. The system consists of polystyrene disposable test rotors, disk dispenser, and CB instrument. Antibiotics are manually dispensed into 15 of the 16 compartments in the test rotor (one compartment is the growth control chamber), and then the rotors are sealed with a flexible ring. The test inoculum is adjusted in sterile saline to the turbidity of a 0.5 McFarland standard. A 100-μl sample of this inoculum and 5 ml of the Roche susceptibility test broth are dispensed into the central compartment of the test rotor, and the rotor is sealed with an adhesive disk. Patient demographic information and the rotor identification number are entered into the system, and then the rotor is placed into the input module of the instrument, which has a capacity for 10 rotors. The rotor is automatically transported into the CB 35°C incubator, where the rotor, with the inoculum in the central reservoir, is incubated for 20 min. The rotor is then moved to the centrifuge-photometer station, where the inoculum is transferred into the 16 cuvette chambers by a series of centrifugation steps. A total volume of 300 μl of fluid is distributed into each of 16 predosing chambers by centrifugation at 500 rpm for 1 s. Then the rotor is centrifuged at 850 rpm for 2 s to transfer the residual fluid into the overflow chamber. When the rate of rotation is increased to 3,000 rpm for 7 s, the inoculum flows from the predosing chambers through Z channels into the cuvette chambers with the antimicrobial agents. After an initial A_{546} reading is recorded, the rotor is automatically transported back into the incubation chamber. The turbidity of every cuvette chamber is then measured at 20-min intervals, for a total of 15 rotor readings. The measured values for each antibiotic are stored in the system and compared with the positive growth control. After the final test readings are completed at 5 h, the rotor is transported to the waste compartment. Another rotor can be immediately inserted into the vacant slot to provide continuous testing with 50 rotors. The system computer calculates the susceptibility of the test organism to the antimicrobial agent from the kinetic measurements and prints the results as susceptible, intermediate, or resistant. If inadequate growth is achieved in the control cuvette, then no susceptibility test results are calculated. Additional data such as the measured absorbance and growth curves can be printed.

Susceptibility test methods. In this study, each organism-antibiotic combination was tested by three methods: the CB system, the Kirby-Bauer disk diffusion (KB) method, and the broth microdilution (BD) method. The CB system was

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used according to the instructions of the manufacturer as described above. The KB and BD tests were performed and interpreted as described by the National Committee for Clinical Laboratory Standards (11, 12). A single lot of Mueller-Hinton agar (GIBCO Diagnostics, Madison, Wis.) was selected after appropriate quality control studies and used for all disk diffusion tests. BD trays were prepared in-house with a single lot of cation-supplemented Mueller-Hinton broth and stored at −80°C for up to 4 weeks. Daily quality control strains were used to ensure proper test performance with the KB and BD methods.

Antimicrobial agents. The antimicrobial agents tested in this study were ones currently available or under development for use in the CB system. A total of 13 antibiotics were tested against gram-positive cocci, and 24 antibiotics were tested against gram-negative bacilli. Table 1 is a listing of all drug concentrations that were tested in the CB system. Each drug was tested by all three susceptibility methods, with the exception of amoxicillin. CB results with amoxicillin were compared with the ampicillin results in the two reference methods.

Organisms. All organisms tested in this study were recent clinical isolates recovered in specimens submitted to the Barnes Hospital Clinical Microbiology Laboratory. A total of 100 gram-positive cocci and 250 isolates of the family *Enterobacteriaceae* were tested. Preliminary studies previously reported indicated that *Pseudomonas* spp. and other nonfermenters could not be tested accurately in the CB system (Murray et al., Abstr. Annu. Meet. Am. Soc. Microbiol. 1985). Therefore, these organisms were excluded from this study. The number of tested organisms from each major genus was determined before initiation of the study to ensure that all groups of commonly encountered organisms would be tested. Selected challenge organisms were not tested in this phase of the study because our purpose was to determine if an acceptable level of performance could be obtained with organisms routinely encountered. If this is not possible, then tests with challenge organisms are not warranted. The organisms tested were 50 isolates of *Staphylococcus aureus*, 25 coagulase-negative staphylococcal isolates (referred to as *Staphylococcus epidermidis* throughout this report), 25 *Enterococcus* isolates, 50 *Escherichia coli* isolates, 42 *Klebsiella pneumoniae* isolates, 8 *Klebsiella oxytoca* isolates, 34 *Enterobacter cloacae* isolates, 13 *Enterobacter aerogenes* isolates, 2 *Enterobacter agglomerans* isolates, 1 *Enterobacter sakazakii* isolate, 23 *Serratia marcescens* isolates, 1 *Serratia liquefaciens* isolate, 1 *Serratia rubidaea* isolate, 25 *Proteus mirabilis* isolates, 12 *Proteus vulgaris* isolates, 17 *Morganella morganii* isolates, 16 *Providencia stuartii* isolates, and 5 *Providencia rettgeri* isolates.

TABLE 1. Antimicrobial agents tested in the CB system

Antimicrobial agent	Labeled disk mass (μg)[a]	Identification	
		Gram-positive	Gram-negative
Amikacin	3.0		X
Amoxicillin	1.5	X	X
Amoxicillin-clavulanic acid	0.4/0.2	X	X
Carbenicillin	2.5		X
Cefazolin	1.5	X	X
Cefoperazone	1.5		X
Cefotaxime	0.75		X
Ceftazidime	0.75		X
Ceftriaxone	0.75		X
Cefuroxime	3.0	X	X
Cephalothin	0.5	X	X
Chloramphenicol	1.5		X
Cinoxacin	6.0		X
Erythromycin	1.0	X	
Gentamicin	1.0	X	X
Minocycline	0.75	X	X
Moxalactam	0.75		X
Netilmycin	3.0	X	X
Nitrofurantoin	4.0		X
Norfloxacin	0.75	X	X
Oxacillin	1.5	X	
Piperacillin	4.0	X	X
Tetracycline	0.75		X
Ticarcillin	20.0		X
Tobramycin	1.0		X
Trimethoprim	1.5	X	X

[a] Amount of antibiotic eluted from the disk into 300 μl of test medium.

RESULTS

A summary of the evaluation of the CB system is presented in Table 2. Complete agreement between the results of the CB and the reference methods was observed for 83 to 85% of the CB-KB comparisons and 77 to 85% of the CB-BD comparisons. Major or very major discrepancies were observed with 5 to 11% of the CB-KB and CB-BD comparisons. In contrast, when the KB and BD tests were compared, a higher percent complete agreement (87 to 92%) and a lower proportion of major or very major discrepancies (1.5 to 4.3%) were observed.

The traditional analysis of test results with major and very major discrepancies is somewhat misleading. All previous studies have calculated the percent major or very major discrepancies by dividing the number of major or very major discrepancies by the total number of tests performed. This practice underestimates the percentage of significantly discrepant results. A major discrepancy can only be reported for an organism that is susceptible by the reference method and resistant by the test method. Likewise, a very major discrepancy can only be reported for an organism that is resistant by the reference method and susceptible by the test method. Thus, if an organism is always susceptible to an antibiotic by the reference method, very major discrepancies would never be reported with the test method. For this reason the percentage of test results with major and very major discrepancies was recalculated.

The susceptibility results for each organism-antibiotic combination tested with the three methods, as well as calculations of the percent agreement and minor, major, and very major discrepancies, are summarized in Tables 3 and 4. Major discrepancies were observed with the CB system for 5.1 to 6.6% of the organisms classified as susceptible by the KB method and 4.0 to 6.5% of the organisms susceptible in BD tests. In contrast, major discrepancies were observed with only 3.0% of the gram-positive cocci and 0.3% of the gram-negative bacilli tested with the reference methods. Very major discrepancies occurred with 21.2 to 25.1% of the gram-positive cocci and 6.3 to 8.5% of the gram-negative bacilli tested in the CB system. This incidence of very major discrepancies with gram-positive cocci was almost three times larger when compared with the incidences with reference methods (8.2%); however, the incidence of very major discrepancies with gram-negative bacilli was essentially the same (5.6% vs. 6.3 to 8.5%).

Analyses of tests with gram-positive cocci are presented in Tables 5 to 8. Essential agreement (complete agreement and minor discrepancies) was observed in 82 to 92% of the

TABLE 2. Summary of CB evaluation

Method comparison	Organism[a]	No. of tests	% of total tests[b]			
			Agree	Discrepancies		
				Minor	Major	Very major
KB-CB	GPC	1,237	82.8	6.5	4.3	6.5
	GNB	5,727	84.5	10.4	3.7	1.4
BD-CB	GPC	1,241	76.7	11.9	4.0	7.4
	GNB	5,724	84.8	10.4	2.8	2.0
BD-KB	GPC	1,259	87.0	8.7	1.8	2.5
	GNB	5,950	92.2	6.3	0.2	1.3

[a] GPC, Gram-positive cocci; GNB, gram-negative bacilli.
[b] Agree, Both test methods with same results; minor discrepancy, one method with susceptible or resistant result and other method with intermediate result; major discrepancy, reference method (BD for comparisons with KB) result susceptible and CB result resistant (percent represents the proportion of all tests performed that had major discrepancies); very major discrepancy, reference method resistant and CB result susceptible (percent represents the proportion of all tests performed that had very major discrepancies).

CB-KB comparisons and 84 to 92% of the CB-BD comparisons (Table 5). In contrast, comparison of the BD and KB reference methods revealed essential agreement for 94 to 97% of the tests with gram-positive cocci. For all three groups of gram-positive cocci, the percent essential agreement with CB comparisons was 5 to 10% less than the agreement between the reference test methods. Essential agreement was observed with >90% of BD-KB comparisons for all antibiotics tested against gram-positive cocci except for trimethoprim (89.9% essential agreement) and amoxicillin (88.9%). However, <90% essential agreement was reported for 7 of the 13 antibiotics tested in the CB-KB comparisons and 6 antibiotics in the CB-BD comparisons (Table 6). Particularly poor results were seen with amoxicillin, cephalothin, and oxacillin. When compared with BD and KB tests, a greater proportion of major discrepancies was observed with *S. aureus* strains tested with the CB system (Table 7). In contrast, the percent major discrepancies with *S. epidermidis* and *Enterococcus* spp. was approximately equal for the three comparisons. Very major discrepancies were more common with all gram-positive cocci tested in the CB system (Table 7). For example, 43 to 44% of the *S. epidermidis* test results in the CB system were falsely classified as susceptible, compared with 8.8% of the results with the reference methods. Major discrepancies were observed with <10% of all antibiotics tested in the BD-KB comparisons except for amoxicillin (Table 8). In contrast, major discrepancies were reported for >10% of the CB tests with amoxicillin, cefazolin, cefuroxime, gentamicin, and oxacillin. Very major discrepancies were also common with virtually all antibiotics tested against gram-positive cocci with the CB system.

TABLE 3. Susceptibility test results[a] with 100 gram-positive cocci

Result	No. of results with method:					
	CB			KB		
	S	I	R	S	I	R
BD						
S	681	23	49	724	12	23
I	77	2	43	58	30	32
R	92	5	269	31	8	341
KB						
S	729	25	53			
I	36	2	15			
R	80	4	293			

[a] S, Susceptible; I, intermediate; R, resistant. For CB-BD comparison: agreement, 952/1,241 (76.7%); minor discrepancies, 148/1,241 (11.9%); major discrepancies, 49/753 (6.5%); very major discrepancies, 92/366 (25.1%). For CB-KB comparison: agreement, 1,024/1,237 (82.8%); minor discrepancies, 80/1,237 (6.5%); major discrepancies, 53/807 (6.6%); very major discrepancies, 80/377 (21.2%). For BD-KB comparison: agreement, 1,095/1,259 (87%); minor discrepancies 110/1,259 (8.7%); major discrepancies, 23/759 (3.0%); very major discrepancies, 31/380 (8.2%).

TABLE 4. Susceptibility test results[a] with 250 gram-negative bacilli

Result	No. of results with method					
	CB			KB		
	S	I	R	S	I	R
BD						
S	3,726	190	162	4,096	85	13
I	107	65	154	102	125	109
R	112	145	1,063	80	77	1,263
KB						
S	3,738	218	211			
I	128	41	112			
R	81	140	1,058			

[a] S, Susceptible; I, intermediate; R, resistant. For CB-BD comparison: agreement, 4,854/5,724 (84.8%); minor discrepancies, 596/5,724 (10.4%); major discrepancies, 162/4,078 (4.0%); very major discrepancies, 112/1,320 (8.5%). For CB-KB comparison: agreement, 4,837/5,727 (84.5%); minor discrepancies, 598/5,727 (10.4%); major discrepancies 211/4,167 (5.1%); very major discrepancies, 81/1,279 (6.3%). For BD-KB comparison: agreement, 5,484/5,950 (92.2%); minor discrepancies, 373/5,950 (6.3%); major discrepancies, 13/4,194 (0.3%); very major discrepancies, 80/1,420 (5.6%).

The results of susceptibility tests of 250 isolates of *Enterobacteriaceae* are presented in Tables 9 to 12. Essential agreement between the reference methods and the CB system was >90% for all groups of gram-negative bacilli (Table 9). However, minor discrepancies were seen for >10% of the tests with *Enterobacter* species, *Serratia* species, *P. vulgaris*, and *M. morganii* (data not shown). In contrast, essential agreement was observed with 96.0 to 99.5% of the BD-KB comparisons, and all groups had <5% minor discrepancies.

Essential agreement was observed for >96% of BD-KB comparisons for all antibiotics tested against gram-negative bacilli except for amoxicillin-clavulanic acid (88.0%). However, <90% essential agreement was reported for amoxicillin (87.1%), cephalothin (78.0%), and minocycline (82.5%) in the CB-KB comparisons and for amoxicillin-clavulanic acid (83.5%), cefoperazone (88.3%), and cephalothin (82.7%) in the CB-BD comparisons (Table 10). Additionally, minor discrepancies were observed for >10% of the CB-reference

TABLE 5. Analysis of essential agreement (by organism) of susceptibility tests of gram-positive cocci

Organism(s)	% of tests with essential agreement[a] for comparison:		
	BD-KB	CB-KB	CB-BD
Staphylococcus aureus	96.0	90.0	88.9
Staphylococcus epidermidis	93.6	82.4	84.1
Enterococcus spp.	97.4	92.2	92.3

[a] Essential agreement: complete agreement and minor discrepancies.

TABLE 6. Analysis of essential agreement (by antibiotic) of susceptibility tests of gram-positive cocci

Antimicrobial agent	% of tests with essential agreement[a] for comparison:		
	BD-KB	CB-KB	CB-BD
Amoxicillin	88.9	77.3	80.4
Amoxicillin-clavulanic acid	96.0	91.8	92.8
Cefazolin	93.0	86.6	90.7
Cefuroxime	96.0	90.7	90.8
Cephalothin	97.0	80.7	79.6
Erythromycin	93.4	86.3	80.0
Gentamicin	99.0	85.6	88.6
Minocycline	100	89.7	90.7
Netilmycin	100	96.9	97.9
Norfloxacin	99.0	100	97.9
Oxacillin	93.9	85.5	80.4
Piperacillin	97.9	95.9	98.0
Trimethoprim	89.9	91.8	84.5

[a] Essential agreement: complete agreement and minor discrepancies.

method comparisons for 8 of the 24 antibiotics (data not shown).

Major discrepancies were very uncommon for the BD-KB comparisons but were observed with >5% of the CB-reference method comparisons with *P. vulgaris*, *M. morganii*, and *Providencia* spp. (Table 11). Very major discrepancies were reported for >5% of the BD-KB tests with *Klebsiella* spp. and *Proteus mirabilis*; CB-KB tests with *Klebsiella* spp., *Enterobacter* spp., and *P. vulgaris*; and CB-BD tests with *Klebsiella* spp., *Enterobacter* spp., *P. mirabilis*, and *P. vulgaris*. Major discrepancies were observed for <2% of all antibiotics tested in the BD-KB comparisons except for minocycline (12.3%). In contrast, major discrepancies were reported for >10% of the CB tests with amoxicillin, cefoperazone, cephalothin, nitrofurantoin, and piperacillin (Table 12). Very major discrepancies were also commonly observed with CB tests, particularly with amoxicillin-clavulanic acid, ceftazidime, gentamicin, minocycline, and ticarcillin.

DISCUSSION

The CB system is a highly automated system for performing antimicrobial susceptibility tests and bacterial identifications in 5 h. During the course of these studies, the operation of the system was very reliable, with no significant mechanical or software problems encountered. Processing of specimens was totally automated after the test inoculum was prepared and poured into the rotor reservoir. Reproducibility of the tests was excellent, with essentially identical results obtained with the quality control organisms throughout the course of the study.

TABLE 7. Analysis of major and very major discrepancies (by organism) of susceptibility tests of gram-positive cocci

Organism(s)	% Major discrepancies[a] for comparison:			% Very major discrepancies[b] for comparison:		
	BD-KB	CB-KB	CB-BD	BD-KB	CB-KB	CB-BD
Staphylococcus aureus	0.3	7.4	5.4	11.8	17.4	24.5
Staphylococcus epidermidis	6.1	6.9	9.1	8.8	43.7	42.9
Enterococcus spp.	6.6	3.7	6.5	0	14.2	15.8

[a] Percent major discrepancies is the proportion of susceptible organisms as determined by the reference method that was classified as resistant by the test method.

[b] Percent very major discrepancies is the proportion of resistant organisms as determined by the reference method that was classified as susceptible by the test method.

TABLE 8. Analysis of major and very major discrepancies[a] (by antibiotic) of susceptibility tests of gram-positive cocci

Antimicrobial agent	% Major discrepancies for comparison:			% Very major discrepancies for comparison:		
	BD-KB	CB-KB	CB-BD	BD-KB	CB-KB	CB-BD
Amoxicillin	16.7	18.9	13.5	7.0	25.0	24.6
Amoxicillin-clavulanic acid	4.2	6.0	8.6	3.7	13.3	11.1
Cefazolin	7.8	18.2	10.3	9.1	3.6	15.0
Cefuroxime	4.4	10.0	15.4	4.1	9.5	2.6
Cephalothin	2.0	2.3	4.6	4.9	32.1	38.3
Erythromycin	0	0	0	11.1	31.3	38.5
Gentamicin	0	10.3	9.7	8.3	41.2	33.3
Minocycline	0	1.4	1.5	0	34.6	32.0
Netilmycin	0	1.1	0	0	100	100
Norfloxacin	0	0	0	100	0	100
Oxacillin	9.9	29.0	34.2	3.5	5.2	10.2
Piperacillin	0	5.4	1.5	15.4	0	7.7
Trimethoprim	2.7	0	0	32.0	47.1	62.5

[a] For calculation of percent major and very major discrepancies, see Table 7, footnotes *a* and *b*, respectively.

The overall complete agreements for the CB-KB and CB-BD comparisons with gram-positive cocci were 82.7 and 76.7%, respectively (Table 2). A large number of minor discrepancies (25.8%) for CB-BD comparisons of *Enterococcus* spp. was primarily responsible for the reduced overall complete agreement of the CB-BD comparisons. The lowest correlation between the reference methods and the CB system was seen with *S. epidermidis* (Table 5). We also experienced some difficulty in obtaining adequate growth of many isolates of *S. epidermidis* in the CB system, which partially explains the testing discrepancies.

Discrepancies between the reference methods and CB tests with gram-positive cocci were common with some antibiotics: minor discrepancies with gentamicin, norfloxacin, oxacillin, piperacillin, and erythromycin; major discrepancies with oxacillin, cefazolin, and amoxicillin; very major discrepancies with amoxicillin, cephalothin, erythromycin, gentamicin, minocycline, and trimethoprim (Table 8). Additionally, very major discrepancies were reported for all CB tests with netilmycin and norfloxacin, although only a few gram-positive cocci were resistant to these antibiotics.

TABLE 9. Analysis of essential agreement (by organism) of susceptibility tests of gram-negative bacilli

Organism(s)	% of tests with essential agreement[a] for comparison:		
	BD-KB	CB-KB	CB-BD
Escherichia coli	99.5	96.2	96.6
Klebsiella spp.	96.0	95.8	94.6
Enterobacter spp.	98.9	94.3	95.4
Serratia spp.	99.4	97.9	97.1
Proteus mirabilis	99.2	96.8	96.5
Proteus vulgaris	98.6	91.5	90.3
Morganella morganii	99.0	93.0	93.6
Providencia spp.	98.0	91.8	92.9

[a] Essential agreement: complete agreement and minor discrepancies.

TABLE 10. Analysis of essential agreement (by antibiotic) of susceptibility tests of gram-negative bacilli

Antimicrobial agent	% of tests with essential agreement[a]		
	BD-KB	CB-KB	CB-BD
Amikacin	100	98.0	97.9
Amoxicillin	96.0	87.1	91.3
Amoxicillin-clavulanic acid	88.0	92.1	83.5
Carbenicillin	97.6	96.5	95.4
Cefazolin	98.4	95.5	95.9
Cefoperazone	99.2	91.7	88.3
Cefotaxime	100	99.1	98.8
Ceftazidime	99.2	91.3	91.7
Ceftriaxone	100	100	99.6
Cefuroxime	100	93.8	93.8
Cephalothin	98.8	78.0	82.7
Chloramphenicol	97.6	100	98.3
Cinoxacin	100	100	100
Gentamicin	100	99.2	98.8
Minocycline	97.2	82.5	95.0
Moxalactam	100	99.6	99.6
Netilmycin	100	100	100
Nitrofurantoin	100	92.1	98.3
Norfloxacin	99.6	100	100
Piperacillin	96.8	92.2	93.3
Tetracycline	99.2	98.3	95.9
Ticarcillin	97.6	95.5	90.0
Tobramycin	99.2	98.8	98.8
Trimethoprim	98.4	98.7	99.6

[a] Essential agreement: complete agreement and minor discrepancies.

The overall agreement between the CB and the reference methods for members of the *Enterobacteriaceae* was 85% (Table 2). Minor discrepancies were commonly reported for all genera, although major and very major discrepancies were less common and primarily restricted to specific organism-antibiotic combinations. The antibiotics most commonly associated with discrepancies were: minor discrepancies with amoxicillin-clavulanic acid, cefuroxime, chloramphenicol, minocycline, nitrofurantoin, and tetracycline; major discrepancies with amoxicillin and cephalothin; very major discrepancies with amoxicillin-clavulanic acid, ceftazidime, gentamicin, minocycline, and ticarcillin (Table 12). Approximately 40% of strains identified as amoxicillin susceptible (including the majority of *P. mirabilis* isolates) were classified as resistant with the CB system, and 75% of the *Enterobacteriaceae* members defined as resistant to amoxicillin-clavulanic acid with the reference methods were classified as either susceptible or intermediate with the CB system. Likewise, discrepancies were commonly observed with other penicillins: piperacillin with *M. morganii* (susceptible strains classified as resistant or intermediate) and ticarcillin with *Klebsiella* spp. and *P. vulgaris* (resistant strains classified as susceptible or intermediate). More than 50% of all cephalothin-susceptible isolates (including 87% of *E. coli* isolates) were classified as intermediate or resistant by the CB system. Discrepancies with the testing of broad-spectrum cephalosporins involved strains defined as susceptible by the reference methods and as either intermediate or resistant by the CB system. This was seen most commonly with cefoperazone and ceftazidime and was primarily associated with isolates of *M. morganii*, *Providencia* spp., and *P. vulgaris*. Discrepancies were less commonly seen with the other species. Finally, approximately 50% of all isolates resistant to minocycline were classified as susceptible or intermediate with the CB system, and the majority of the nitrofurantoin-susceptible isolates were misclassified.

The true incidence of major and very major discrepancies reported in this study cannot be directly compared with the incidences found for other automated susceptibility testing systems, because data on the number of organisms susceptible or resistant by the reference methods are not generally described for the other systems. However, the overall performance of the CB system in this study was below the performances previously reported for the Autobac and MS-2 systems (5, 9, 14, 15) and superior to the performance observed in initial susceptibility studies with the Vitek AMS system (5, 9). More recent studies (10, 17) with the Vitek AMS system with selected gram-negative bacilli and a limited number of antibiotics have reported between 91.5 to 97.7% essential agreement with a reference method. This is

TABLE 11. Analysis of major and very major discrepancies[a] (by organism) of susceptibility tests of gram-negative bacilli

Organism(s)	% Major discrepancies for comparison:			% Very major discrepancies for comparison:		
	BD-KB	CB-KB	CB-BD	BD-KB	CB-KB	CB-BD
Escherichia coli	0.1	0.1	3.7	2.9	2.4	3.5
Klebsiella spp.	1.0	4.5	2.2	16.8	13.3	20.4
Enterobacter spp.	0	4.1	2.9	3.9	11.2	10.1
Serratia spp.	0	2.7	2.2	1.9	1.5	4.2
Proteus mirabilis	0	3.3	3.4	8.6	2.7	6.8
Proteus vulgaris	0.6	9.5	9.3	3.2	8.9	12.3
Morganella morganii	0	9.6	8.6	3.7	2.5	2.8
Providencia spp.	0.7	14.1	11.3	3.8	1.4	2.1

[a] For calculation of percent major and very major discrepancies, see Table 7, footnotes *a* and *b*, respectively.

TABLE 12. Analysis of major and very major discrepancies[a] (by antibiotic) of susceptibility tests of gram-negative bacilli

Antimicrobial agent	% Major discrepancies for comparison:			% Very major discrepancies for comparison:		
	BD-KB	CB-KB	CB-BD	BD-KB	CB-KB	CB-BD
Amikacin	0	2.1	2.1	0	0	0
Amoxicillin	1.8	44.8	35.2	4.8	0.6	1.1
Amoxicillin-clavulanic acid	1.3	3.7	5.2	19.1	13.3	25.2
Carbenicillin	0	6.4	2.5	4.8	2.8	6.7
Cefazolin	0	8.4	7.1	3.5	0	0.9
Cefoperazone	0	9.1	11.7	22.2	0	14.3
Cefotaxime	0	0.9	0.9	0	0	20.0
Ceftazidime	0	8.5	7.7	2.5	25.0	28.6
Ceftriaxone	0	0	0.4	0	0	0
Cefuroxime	0	8.7	8.7	0	0	0
Cephalothin	0	48.1	42.6	2.4	0.9	0.9
Chloramphenicol	0	0	0	10.9	0	7.6
Cinoxacin	0	0	0	0	0	0
Gentamicin	0	0	0	0	25.0	30.0
Minocycline	12.3	0	0	0	25.3	10.0
Moxalactam	0	0.4	0.4	0	0	0
Netilmycin	0	0	0	0	0	0
Nitrofurantoin	0	12.8	2.9	0	3.7	3.6
Norfloxacin	0.4	0	0	0	0	0
Piperacillin	0	19.6	6.9	14.6	0	6.0
Tetracycline	0	2.6	1.2	1.5	1.6	6.9
Ticarcillin	0	1.3	0	5.8	11.4	24.7
Tobramycin	0	1.1	0.6	11.1	0	14.3
Trimethoprim	1.4	0.5	0	3.3	6.9	3.7

[a] For calculation of percent major and very major discrepancies, see Table 7, footnotes *a* and *b*, respectively.

similar to the 95% essential agreement reported for the CB system with gram-negative bacilli in this study. It should be noted, however, that the CB system cannot be used for tests with *Pseudomonas* spp. or other nonfermentative gram-negative bacilli at the present time.

Despite the large number of minor, major, and very major discrepancies observed with the CB system, many of these should be eliminated with additional modifications of the current system. For example, the system computer should be programmed to interpret as resistant all cephalosporin results with oxacillin-resistant staphylococci. The antimicrobial agent contents in the disks should be changed to reduce the number of discrepancies observed with consistent trends towards resistant (content too low) or susceptible (content too high). Finally, an increase in the incubation period should resolve the problems encountered with delayed growth (false susceptibility) with broad spectrum cephalosporins tested against gram-negative bacilli. If these modifications lead to an improved performance, then this highly automated, rapid system should warrant additional clinical studies.

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