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Comparative Evaluation of Four Systems for Determining Susceptibility of Gram-Positive Organisms

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A study was undertaken to compare four commercial systems for testing the antimicrobial susceptibility patterns of gram-positive cocci. The reference method was an agar dilution method. The systems evaluated were the MS-2 system (Abbott Diagnostics Div., Mississauga, Ontario), the AutoMicrobic system (AMS) (Vitek Systems, Inc., Hazelwood, Mo.) with the gram-positive susceptibility (GPS) card, the Sceptor system (BBL Microbiology Systems, distributed by Becton Dickenson, Canada Inc., Mississauga, Ontario), and the Micro-Media system (Beckman Instruments, Inc., Anaheim, Calif.). There was a >98% essential accord (EA) between all test results and the reference method results when testing 134 isolates of *Staphylococcus aureus*. In testing 79 isolates of coagulase-negative staphylococci the EA was >97% with all systems except the MS-2. In the MS-2 system only, 30% of tests were interrupted by the instrument because of insufficient growth in the control chamber. Excluding the Sceptor system, the EA was >96% on testing 70 isolates of enterococcus. In testing 15 isolates of group B *Streptococcus* there was 91% EA with the AMS and Sceptor systems and only 71 and 88% EA with the MS-2 and Micro-Media systems, respectively. The new AMS GPS MIC card was tested against 29 methicillin-resistant *S. aureus*, 10 coagulase-negative staphylococci, and 9 enterococci, and it gave more accurate results than the earlier GPS breakpoint card. The Micro-Media and MS-2 systems did not reliably detect marginally methicillin-resistant *S. aureus*. The MS-2 was the least expensive system to operate on a cost per test basis ($3.59 Can.), whereas the Sceptor was the most expensive system ($5.29 Can.). The AMS was the least labor intensive (0.9 min per test), and the Sceptor system was the most time consuming (2.9 min per test).

In our laboratory the MS-2 system (Abbott Diagnostics Div., Mississauga, Ontario) has given unsatisfactory results in susceptibility testing of staphylococci. Because of this problem all gram-positive susceptibility tests are performed by agar disk diffusion. Because it is inconvenient and inefficient to use several susceptibility testing formats, we decided to evaluate other automated and semiautomated procedures. We were also concerned with the emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) and with the ability of the various systems to detect the organism. Therefore, we decided to test the different systems with a selection of gram-positive cocci isolated in our hospital.

MATERIALS AND METHODS

The systems loaned to us for evaluation were the Sceptor system from BBL Microbiology Systems distributed by Becton Dickinson, Canada Inc., Mississauga, Ontario; Micro-Media systems from Beckman Instruments, Inc., Anaheim, Calif.; and the AutoMicrobic system (AMS) from Vitek Systems, Inc., Hazelwood, Mo. In-house was the MS-2 system.

The organisms tested were collected in the routine microbiology laboratory of the Vancouver General Hospital (one isolate per patient) and frozen at −20°C in Trypticase soy broth (BBL) with 5% dimethyl sulfoxide. The isolates were subcultured at least two times to blood agar plates before testing. Organisms were identified by morphology, Gram staining, catalase and coagulase production, hemolysis, bile esculin, and hippurate tests, and tolerance to 6.5% salt. The organisms collected consisted of 134 isolates of *S. aureus*, 79 isolates of coagulase-negative staphylococci (CNS), 70 isolates of enterococcus, and 15 isolates of group B *Streptococcus*. At a later date 29 isolates of MRSA were also tested. Four of the isolates were considered marginally resistant with an oxacillin MIC of 4 μg/ml or a methicillin MIC of 16 μg/ml or both by the reference agar dilution method. The four isolates were also retested by other methods, including oxacillin and methicillin microdilution broth with 2% salt (14) and Mueller-Hinton agar plates with 4% salt on oxacillin disks. All other MRSA isolates had oxacillin and methicillin MICs >8 and >16 μg/ml, respectively.

The reference agar dilution method was done with a multiprong replicator according to National Committee for Clinical Laboratory Standards guidelines (8). Organisms were grown for 2 to 4 h in Trypticase soy broth and adjusted to a McFarland standard of 0.5. A further 1 in 10 dilution was made in the replicator wells to achieve a final spot inoculation of approximately 10^4 CFU per spot. Plates were incubated at 35°C overnight.

The antimicrobial agents and dilutions (micrograms per milliliter) used for the agar dilution were: cefazolin sodium, 4, 8, and 16 (Smith Kline & French Laboratories, Philadelphia, Pa.); clindamycin hydrochloride, 1, 2, and 4 (The Upjohn Co., Kalamazoo, Mich.); cloxacillin sodium, 2, 4, and 8; penicillin G, 1, 2, and 4 (Ayerst Laboratories, Montreal, Quebec, Canada); erythromycin, 2, 4, and 8 (Abbott Laboratories Ltd., Montreal, Quebec, Canada); gentamicin, 4 and 8 (Schering Canada, Inc.); methicillin sodium, 2, 4, and 8 (Bristol Myers Canada, Inc.); tetracycline hydrochloride, 4, 8, and 16 (Lederle Laboratories, Pearl River, N.Y.); trimethoprim-sulfamethoxazole (SXT) $\frac{1}{20}$, $\frac{2}{40}$, and $\frac{4}{80}$ (Burroughs Wellcome Ltd., La Salle, Quebec, Canada); and vancomycin, 2, 4, and 8 (Eli Lilly Canada, Inc.). β-Lactamase testing was done with Nitrocefin disks (BBL) (11).

The control strains used were *S. aureus* ATCC 29213

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TABLE 1. Agreement of each system with the reference agar dilution method in testing enterococci (n = 70)[a]

Drug	Agreement among systems																			
	MS-2					Sceptor[b]					Micro-Media					AMS GPS				
	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)
Cephalothin	0	0	0	100	100	0	0	2	92.9	100	0	0	3	95.7	100	0	0	12	82.9	100
Clindamycin	2	0	0	97.1	97.1						0	0	3	100	100	3	0	32	50.0	95.7
Erythromycin	3	2	2	90.0	92.9						0	1	0	98.6	98.6	1	0	24	64.3	98.6
Gentamicin	3	0	9	82.9	95.7	24	0	26	28.6	65.7	0	0	6	91.4	100	0	0	25	64.3	100
SXT	1	1	1	95.7	97.1	2	3	1	91.4	92.9	10	0	1	84.2	85.7					
Vancomycin	0	1	0	98.6	98.6						0	0	0	100	100	0	0	29	58.6	100
Tetracycline	4	0	0	94.2	94.2	2	2	0	94.1	94.1	0	3	1	98.6	100	2	0	3	92.8	97.1
Total or avg	13	4	12	94.1	96.5	28	5	29	76.6	88.5	10	4	14	95.5	97.8	6	0	125	73.2	98.6

[a] Methicillin, penicillin, or oxacillin were not used in the agar dilution reference method.
[b] Urine susceptibility panel.

(positive for beta-lactamase), *S. aureus* ATCC 25923 (negative for beta-lactamase), *S. saprophyticus* ATCC 15305, *Streptococcus faecalis* ATCC 29212, and *Streptococcus agalactiae* ATCC 13813.

Sceptor system gram-positive MIC panels were used for all isolates except for enterococci, which were tested in the MIC panel for urinary isolates. A suspension of each organism was prepared in sterile saline to a 0.5 McFarland standard, and 10 μl was transferred to the Sceptor gram-positive broth with a disposable loop. Panels were inoculated according to the direction of the manufacturer by using the automated preparation station.

Micro-Media Fox gram-positive MIC identification panels were used. A sterile 0.02% Tween 80 solution in distilled water was made in the laboratory and dispensed in 10-ml amounts. A 2- to 3-h culture grown in Trypticase soy broth and adjusted to a McFarland standard of 0.5 was diluted in the 0.02% Tween 80 solution, and the panels were inoculated according to the directions of the manufacturer. Both the Micro-Media and Sceptor panels were incubated at 35°C overnight and were read with the reader-recorder module of the respective manufacturer.

The breakpoint gram-positive susceptibility (GPS) card (product 51-1405) and software disk (AMSP 13 ROB; Vitek) were used in the AMS tests. The manufacturer supplied a commercial 0.45% saline solution to use as the diluent. The inoculum (McFarland standard, 0.5) was made from a fresh overnight culture of the organism grown on blood agar (Prepared Media Laboratories, Richmond, British Columbia, Canada), and the cards were set up according to the directions of the manufacturer. After this study was completed, the manufacturer supplied its most recent MIC card called GPS-M (product 51-1410; Vitek). This card was used instead of the breakpoint GPS card for testing the MRSA collection. The GPS-M card was also used to check some of the more discrepant results that occurred with the GPS card in the CNS and enterococci results. The GPS-M card was tested with a software disk (AMSP 14 ROA; Vitek).

In the MS-2 system the GPS cartridge was used with the MS-2 Isosensitest broth (Abbott). Erythromycin enzyme inducer (0.1 ml) was added to all tests. The MS-2 system used program software 03.02.

Discrepancies among reference and test methods were categorized as very major (VM) error, in which the test result was susceptible when the reference method was resistant; major (MA) error, in which the test result was resistant when the reference method was sensitive; and minor (MI) error, in which the difference between the test and reference results involved an intermediate result (14). Complete accordance (CA) was calculated with the formula $CA = [n - (VM + MA + MI)/n] \times 100$, and essential accordance (EA) was calculated from the formula $EA = [n - (VM + MA)/n] \times 100$.

Reproducibility and time studies. All four gram-positive reference strains, *S. aureus* ATCC 29213, *S. saprophyticus* ATCC 15305, *Streptococcus faecalis* ATCC 29212, and *Streptococcus agalactiae* ATCC 13813 were tested 5 or 10 times on different days with each system to test the reproducibility of results. In those systems (Micro-Media, AMS GPS-M, and Sceptor) that gave discrete MIC values, reproducibility was defined as being within one dilution above or below the reference method result. The MS-2 and AMS GPS cards that listed the results as susceptible, intermediate, or resistant were evaluated according to the reproducibility of the susceptible, intermediate, or resistant calls. Because the MRSA control was used only in the second portion of the study, the MS-2 and Sceptor systems were not tested on a daily basis.

Technical time studies were done to aid in the determination of productivity and cost effectiveness. Steps that were common to all methods were not included, such as preparation of the bacterial inoculum, standardizing to McFarland 0.5, and preparation of purity plates. Micro-Media tests required a 2- to 3-h broth incubation step, whereas the other inocula were made in saline from fresh cultures.

RESULTS

There were 70 isolates of enterococci tested with the four systems (Table 1). The AMS GPS card gave the fewest VM and MA errors, but the greatest number of MI errors, and consequently the highest EA and lowest CA. Although the Micro-Media and MS-2 results appear similar, there was a significant difference ($P \leq 0.05$) when the standard error of difference between percentages was calculated. The EA for the AMS was significantly greater than that for the Micro-Media system ($P \leq 0.05$). The Sceptor urine isolate panel gave unacceptable results. The greatest number of errors in all systems occurred with gentamicin and SXT (SXT is not included in the AMS panel).

When the 15 group B streptococci were compared (Table 2), the Sceptor and AMS gave the best results, with no significant differences between their respective CA and EA. The MS-2 and Micro-Media systems gave poor results.

TABLE 2. Agreement of each system with the reference agar dilution method in testing group B streptococci (n = 15)[a]

Drug	Agreement among systems[b]																			
	MS-2					Sceptor					Micro-Media					AMS GPS				
	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)
Cephalothin	0	0	0	100	100	0	0	0	100	100	0	0	0	100	100	0	0	0	100	100
Clindamycin	0	0	0	100	100	0	1	0	93.3	93.3	0	0	0	100	100	0	0	0	100	100
Erythromycin	0	0	2	86.7	100	0	1	0	93.3	93.3	0	0	0	100	100	0	0	0	100	100
Gentamicin	0	14	0	6.6	6.6	1	0	1	86.7	93.3	0	5	6	26.7	66.7	0	8	0	46.7	46.7
Methicillin	0	10			33.3	0	0			100	0	0			100					
Penicillin	0	2			86.7	0	0			100	0	0			100	0	0			100
SXT	0	3	4	53.3	80.0	1	3	0	71.4	71.4	8	0	3	26.7	46.7					
Tetracycline	5	1	4	33.3	60.0	1	1	0	86.7	86.7	1	0	1	86.7	93.3	0	0	4	73.3	100
Total or avg	5	30	10	64.2	70.8	3	6	1	91.7	92.5	9	5	10	80.0	88.3	0	8	4	88.6	92.4

[a] Vancomycin was not used in the agar dilution reference method.
[b] VM, Test results resistant, truly susceptible; MA, test results susceptible, truly resistant; MI, erroneous results featuring an intermediate result either in the test or in the reference method.

Again, the greatest number of errors in all systems occurred with tests of gentamicin and SXT.

The results of tests of 79 isolates of CNS were tabulated (Table 3). In the MS-2 system 24 tests were stopped because of insufficient growth. Each of the other systems had one test that failed because of poor growth. The error columns list errors found in growing tests only.

The EA observed with the AMS was significantly better than that of the MS-2, Micro-Media, or Sceptor systems ($P \leq 0.01$). There was no significant difference between the Micro-Media and Sceptor systems. The MS-2 gave poorer results than the other systems. When the CA was examined, the AMS had many MI errors with vancomycin (but no MA errors) which lowered its overall CA to less than that of the MS-2 system. The Sceptor and Micro-Media systems performed equally well. Most errors in the Sceptor, Micro-Media, and AMS systems (other than with vancomycin) were seen with gentamicin.

The results of tests with 134 isolates of methicillin-susceptible *S. aureus* are presented in Table 4. All systems compared favorably, having CA greater than 96% and EA greater than 98%. However the EA and CA observed with the MS-2 and Sceptor systems were significantly less than those of the Micro-Media and AMS methods ($P \leq 0.01$), with most of the errors occurring with penicillin and SXT. The MA errors that occurred with penicillin tests in the Sceptor system were because of beta-lactamase-negative *S. aureus* being called resistant at dosages of 0.25 μg/ml. There was no significant difference between the MS-2 and Sceptor systems and between the Micro-Media and AMS systems.

The 29 MRSA were tested with the new AMS GPS-M (Table 5). Because all systems had a disclaimer that cephalothin results may be unreliable with MRSA, this drug was excluded from the analysis. SXT was not used in the reference agar dilution method. Although the EA in all systems was greater than 95%, the AMS was significantly better ($P \leq 0.01$) than its nearest competitor, the Micro-Media system. The Sceptor system detected all 29 MRSA isolates. The AMS missed one of the marginally resistant isolates, whereas the MS-2 and Micro-Media systems missed three and four of the marginally resistant isolates, respectively. The MS-2 system also did not detect three of the more resistant isolates.

The preceding information was summarized by comparing the number of errors and the CA and EA of each system by organism tested (Table 6). The agreement among each system by antimicrobial agent was also summarized (Table 7). All antimicrobial agents were not tested against all organisms. The calculations for the MS-2 system do not include the 24 CNS whose tests did not proceed to completion. The greatest number of discrepancies occurred with gentamicin and SXT. The MS-2 system also performed poorly in testing

TABLE 3. Agreement of each system with the reference agar dilution method in testing CNS (n = 79)

Drug	Agreement among systems[a]																			
	MS-2					Sceptor					Micro-Media					AMS GPS				
	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)
Cephalothin	0	0	2	97.4	100	0	1	4	93.5	98.7	4	0	1	93.7	94.9	1	0	0	98.7	98.7
Clindamycin	0	3	2	93.7	96.2	1	4	1	92.2	93.5	0	0	2	97.5	100	2	0	1	96.2	97.4
Erythromycin	0	3	4	91.1	96.2	1	3	0	94.8	94.8	0	0	0	100	100	1	0	3	94.9	98.7
Gentamicin	1	1	3	93.7	97.4	1	0	6	90.9	98.7	2	0	7	88.6	97.5	2	1	4	91.1	96.2
Oxacillin																1	0			98.7
Methicillin	1	13			82.3	3	2			93.4	1	7			89.7					
Penicillin	3	1			94.9	0	1			98.7	1	1			97.4	0	0			100
SXT	0	8	8	79.7	89.9	0	6	5	85.7	92.2	1	0	7	89.9	98.7	0	0			
Vancomycin	0	0	0	100	100	0	0	0	100	100	0	0	0	100	100	0	0	65	17.7	100
Tetracycline	4	2	2	89.9	92.4	0	0	2	97.4	100	3	0	3	92.4	96.2	3	0	4	91.1	96.2
Total or avg	9	31	21	87.7	91.9	6	17	18	94.2	96.7	12	8	20	94.3	97.2	10	1	77	85.9	98.2

[a] See Table 2, footnote *b*.

TABLE 4. Agreement of each system with the reference agar dilution method in testing methicillin-susceptible *S. aureus* (n = 134)

Drug	Agreement among systems[a]																			
	MS-2					Sceptor					Micro-Media					AMS GPS				
	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)
Cephalothin	0	0	0	100	100	0	1	0	99.3	99.3	0	0	0	100	100	0	0	0	100	100
Clindamycin	0	2	0	98.5	98.5	0	1	0	99.3	99.3	2	0	0	98.5	98.5	1	0	0	99.3	99.3
Erythromycin	0	1	5	95.5	99.3	0	1	6	94.8	99.3	1	0	2	97.8	99.3	0	0	2	98.5	100
Gentamicin	0	1	4	97.0	99.2	0	0	2	98.5	100	0	0	2	98.5	100	0	0	0	100	100
Methicillin	0	0			100	0	1			99.3	0	0			100					
Oxacillin																0	0			100
Penicillin	3	5			94.0	1	14			88.8	0	0			100	0	0			100
SXT	0	6	10	88.1	95.5	0	3	2	96.3	97.8	0	0	1	99.3	100	0				
Vancomycin	0	0	0	100	100	0	0	1	99.3	100	0	0	0	100	100	0	0	5	96.3	100
Tetracycline	2	1	2	96.3	97.8	0	2	4	95.5	98.5	0	0	1	99.3	100	1	0	2	97.8	99.3
Total or avg	5	16	21	96.5	98.3	1	23	15	96.8	98.0	3	0	6	99.3	99.8	2	0	9	99.0	99.8

[a] See Table 2, footnote *b*.

methicillin (EA, 87.1%). The AMS showed a large number of MI errors in testing clindamycin, erythromycin, and vancomycin with the GPS card. All systems had greater than 95% EA for *S. aureus* and enterococci except for the Sceptor system and enterococci. The Sceptor, Micro-Media, and AMS systems had greater than 95% EA for CNS.

The GPS-M card from the AMS was not received until most of the study was completed. The 10 isolates of CNS and 9 isolates of enterococci that had demonstrated several MI errors, especially involving clindamycin, erythromycin, and vancomycin, were retested with the new GPS-M cards. Most of the errors had occurred with an intermediate reading for vancomycin, and all were corrected to susceptible with the GPS-M card; over half the clindamycin and erythromycin errors were corrected. The AMS GPS-M brochure states a disclaimer that: "some antimicrobic-organism combinations may statistically show a higher number of discrepant ($>\pm 1$) MIC calls by the AMS (compared to microdilution MIC). These combinations include: group B *Streptococcus*—gentamicin, tetracycline; group D *Streptococcus*—erythromycin, tetracycline; CNS—gentamicin, tetracycline; *S. aureus*—gentamicin, tetracycline."

The new panel corrected 7 of 12 errors occurring in the disclaimed group. It also corrected 60% of the previous errors, partially corrected 4% of the errors, and did not correct 36% of the errors. Most of these last errors occurred with gentamicin and enterococci. No minor errors occurred with clindamycin, erythromycin, and vancomycin when the GPS-M card was tested against MRSA. The antimicrobial agent-organism combinations that were the subjects of the disclaimer gave results that compared favorably with those seen in other systems.

The category calls used by the different systems did not all agree with National Committee for Clinical Laboratory Standards recommendations (9). The six MS-2 disks that were not as sensitive as was suggested by the National Committee were clindamycin, erythromycin, penicillin, SXT, tetracycline, and vancomycin. The Sceptor and AMS GPS-M cards followed the guidelines exactly. On the other hand, there was an overlapping of very susceptible and moderately susceptible categories of results when cephalothin, gentamicin, vancomycin, ampicillin, and chloramphenicol were tested in the AMS GPS and Micro-Media systems. This category of overlap may explain the low CA seen with the AMS GPS card for vancomycin and gentamicin.

Reproducibility study. Complete accord of results of tests of *S. aureus* ATCC 29213 in the Sceptor system was less than 90% reproducible because of errors in tests with eryth-

TABLE 5. Agreement of each system with the reference agar dilution method in testing MRSA (n = 29)[a]

Drug[b]	Agreement among systems[c]																			
	MS-2					Sceptor					Micro-Media					AMS GPS				
	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)
Clindamycin	0	2	1	89.7	93.1	0	3	0	89.7	89.7	0	0	0	100	100	0	0	0	100	100
Erythromycin	0	0	1	96.4	100	0	1	2	89.3	96.4	0	0	2	92.9	100	0	0	0	100	100
Gentamicin	0	1	0	96.6	96.6	0	3	1	86.2	89.7	0	0	0	100	100	0	0	0	100	100
Methicillin	6	0			79.3	0	0			100	4	0	0	86.2	86.2					
Oxacillin																1	0			96.6
Penicillin	0	0			100	0	0			100	0	0			100	0	0			100
Vancomycin	0	0	0	100	100	0	0	0	100	100	0	0	0	100	100	0	0	0	100	100
Tetracycline	0	0	1	96.6	100	0	0	3	89.7	100	0	0	0	100	100	0	0	0	100	100
Total or avg	6	3	3	94.1	95.5	0	7	6	93.6	96.5	4	0	2	97.0	98.0	1	0	0	100	99.5

[a] SXT was not used in the agar dilution reference method.
[b] Cephalothin not included in statistics.
[c] See Table 2, footnote *b*.

TABLE 6. Summary of results by organism tested in each system

System used	Agreement by organism tested[a]																						Overall mean (%)	
	Methicillin-susceptible *S. aureus* (*n* = 134)					CNS (*n* = 79)				Enterococci (*n* = 70)				*Streptococcus agalactiae* (*n* = 15)				MRSA (*n* = 29)					
	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)	EA (%)	CA	EA
MS-2	5	16	21	96.5	98.3	9	31	21	87.7	91.9	13	4	12	94.1	96.5	5	30	10	64.2	70.8	6	3	3	94.1	95.5	92.5	95.1
Sceptor	1	23	15	96.8	98.0	6	17	18	94.2	96.7	28	5	29	76.6	88.5[b]	3	6	1	91.7	92.5	0	7	6	93.6	96.5	93.0	96.3
Micro-Media	3	0	6	99.3	99.8	12	8	20	94.3	97.2	10	1	11	95.5	97.8	9	5	10	80.0	88.3	4	0	2	87.0	98.0	96.1	98.0
AMS	2	0	9	99.0	99.8	10	1	77	85.9	98.2	6	0	125	73.2	98.8	0	8	4	88.6	92.4	1	0	0	99.5	99.5	90.4	99.1

[a] See Table 2, footnote *b*.
[b] Urine isolate panel.

romycin and chloramphenicol. *Streptococcus agalactiae* ATCC 13813 tests were stopped in the MS-2 because of poor growth in three of eight tests. In those tests that did go to completion, the reproducibility was 68.9%, with most of the errors occurring with gentamicin and SXT. Test results of MRSA in the Micro-Media system were 83.3% reproducible, and there was failure to detect the low-level resistance to methicillin or nafcillin. Overall, the AMS GPS-M card gave the most reproducible results (96.7%), and the AMS GPS was the least satisfactory (88.1%) because of the variability of the results of the *Streptococcus faecalis* control. The MS-2 system also gave poor reproducibility (88.5%) because of the poor performance of the enterococci and *Streptococcus agalactiae*. The Sceptor and Micro-Media systems gave comparable overall results of 93.8% and 95.0% reproducibility, respectively.

Time study. Tests with the AMS were almost three times faster to set up than those with the MS-2 system (Table 8), largely because of the need to make up the MS-2 antimicrobial cartridges and to enter the specimen information into the computer. The AMS had premade panels, and the specimen identification number was put onto the card which was then read by the machine.

The two overnight semiautomated systems, Sceptor and Micro-Media, also differed in time requirements. With the Micro-Media system, a diluent of the inoculum was poured into a tray, and an inoculating head was dipped into the tray and then dipped into the test panel. Specimen entry in the preparation station of the Sceptor system, although slower, was semiautomatic and allowed the operator to simultaneously prepare the next specimen or enter computer information. The manual method of setting up the Sceptor system, with a multi-channel-pipette, required the same time as that allotted to the preparation station.

Cost analysis and system comparison. The Sceptor system was the most expensive to operate, whereas the MS-2 system, after an initial capital outlay, was the least expensive (Table 9). Both had extended 12-month shelf lives of materials, which was an advantage over the AMS and Micro-Media systems, because bulk orders can reduce costs (Table 10). The frozen Micro-Media panels required prompt, direct shipping and storage in a non-frost-free −20°C freezer.

All systems offered custom-designed panels, the MS-2 being immediately adjustable with the alteration of antibiotic disks, whereas the other systems required several weeks to a few months to adjust to a different formula and would involve a minimum purchase order.

The Sceptor and Vitek systems included a beta-lactamase test on their panels. The beta-lactamase well on the Sceptor panel required a heavier inoculum than the other wells and had to be read after 1 h, steps that required extra time (which were not included in the time study).

DISCUSSION

All systems performed well, with each system having weaknesses and strengths that had to be carefully weighed before arriving at a decision to purchase.

The study was undertaken to find a replacement for the MS-2 system which had proved unsatisfactory in testing CNS. As this study has shown, the MS-2 system also detected less than 80% of the MRSA. The inaccuracy confirms reports of other investigators (3). Jorgensen et al. (6) found the MS-2 system detected 91.6% of all MRSA and 86.8% of *S. aureus* that were marginally resistant to methicillin, whereas the AMS performed 4% better. Other workers found that an updated MS-2 software package that lowered

TABLE 7. Summary by antimicrobial agent of the agreement of each system with the reference agar dilution method for all organisms tested

Drug	Agreement among systems[a]																			
	MS-2 (n = 303)					Sceptor (n = 327)					Micro-Media (n = 327)					AMS (n = 327)				
	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)	VM	MA	MI	CA (%)	EA (%)
Cephalothin	0	0	2	99.3	100	0	2	9	95.9	99.3	4	0	4	97.3	98.7	1	0	12	95.6	99.7
Clindamycin	2	7	3	96.0	97.0	1	9	1	97.7	96.1	2	0	2	98.8	99.4	6	0	33	88.1	98.2
Erythromycin	3	6	14	92.4	97.0	1	6	8	94.1	97.2	1	1	4	98.1	98.7	2	0	30	90.2	99.4
Gentamicin	4	17	16	87.7	93.0	26	3	36	79.9	91.0	2	5	21	91.3	97.8	2	9	29	87.7	96.6
Methicillin	7	23			87.1	3	3			97.6	5	7			95.3					
Oxacillin																2	0			99.2
Penicillin	6	8			94.0	1	15			93.7	1	1			99.2	0	0			100
SXT	1	18	23	84.7	93.1	3	15	8	91.1	93.8	19	0	12	89.8	93.8					
Vancomycin	0	1	0	99.7	99.7	0	0	1	99.6	100	0	0	0	100	100	0	0	99	68.3	100
Tetracycline	15	4	9	90.7	93.7	3	5	9	94.8	97.5	4	0	6	96.9	98.8	6	0	13	94.2	98.2

[a] See Table 2, footnote *b*.

the cutoff point for methicillin-resistance detection from 15 to 5 μg/ml increased the sensitivity to 86 to 98% (3, 4, 6). As of March 1985, 2-μg oxacillin disks were made available for the MS-2. However, without a change in salt concentration the system may not detect *S. aureus* that are marginally resistant to methicillin. Increasing salt in the broth may affect the action of the other antibiotics (15). The MS-2 system was unsatisfactory in testing for group B *Streptococcus*, but it gave an EA of greater than 98% for methicillin-susceptible *S. aureus* and enterococci. Test results of staphylococci were highly reproducible, but only 84% accurate for *Streptococcus faecalis*. The MS-2 had the advantages that one could change the antimicrobial formulary at a moment's notice and disposable supplies that could be ordered in bulk. The broth was available in liquid or dry form. Daily maintenance involved the tedious and time-consuming examination of transmittance values. A computer program should be available to perform this function and identify malfunction. The initial capital outlay may be prohibitive to small laboratories. However, the MS-2 system can be used to screen urine samples and to identify members of the family *Enterobacteriaceae*, the more common nonfermenters and yeasts (available on the updated Avantage module) (17). The MS-2 system may be attractive to the large hospital willing to use alternate methods for the isolation of streptococci and MRSA (3, 5–7).

The Sceptor system performed very well in testing for gram-positive bacteria, including MRSA. Other investigators have found that the Sceptor system detected only 85% of the MRSA (1, 4). The report sheet for gram-positive susceptibilities had a disclaimer that amikacin and gentamicin MICs should not be reported for enterococci. On the advice of the company representative, the urine isolate MIC panel was used for enterococci, because it included a higher concentration range of antimicrobial agents. This panel did not include erythromycin, clindamycin, or vancomycin. The EA for gentamicin was 65.7%, making the use of the urine isolate MIC panel inadvisable. The Sceptor kits were the most expensive to purchase. However, the ability to store the panels at room temperature is an attractive feature. If antimicrobial MICs were not performed frequently, the extended shelf life of the product would be important. The test panel could be set up and read manually if the work load was not sufficient to justify the purchase of the automated preparation station and reader.

The Micro-Media system performed well except that it missed some isolates of *S. aureus* that were marginally resistant to methicillin, a finding that confirms the observations of other investigators (1, 4). It is now recommended that MRSA inocula be prepared from an overnight culture and not from a 2-h broth (9). The frozen panels had a shorter shelf life than the Sceptor or MS-2 systems, but if work volume was sufficient, there would be little wastage. Non-frost-free freezers must be used, as evaporation may occur. The panels were easy to set up and could be read manually or with the reader module. If more than five panels were being tested daily, we would recommend the purchase of reader modules or a magnifying light box because the printing and the wells on the panel are very small.

The AMS performed well for all organisms tested. For some organism-antimicrobial agent combinations there were large discrepancies between EA and CA. These were most notable with enterococci and with the vancomycin test results for CNS. These errors probably occurred as a result of the wide intermediate areas on the GPS cards that did not always agree with the recommendations of the National Committee for Clinical Laboratory Standards. The new GPS-M card with discrete MICs was shown upon limited testing to correct most of these MI errors. The AMS GPS-M with oxacillin and 2% salt detected 96.6% of the MRSA. Other investigators who used the GPS card found the AMS

TABLE 8. Time required to set up and read a test in each of the systems

Procedure	Time (min) required for each system			
	MS-2	Sceptor	Micro-Media	AMS
Set up	2.5	2.2	0.9	0.9
Read	Automatic	0.7	0.9	Automatic
Total	2.5	2.9	1.8	0.9

TABLE 9. Cost analysis by system

System	Cost (1984 Canadian dollars)				
	Capital cost (automated)	With data management	GPS panel	Broth and disposables	Technician cost/test (at $13.00/h)
MS-2	160,000		2.70	0.35	0.54
Sceptor	13,165	28,865	3.57	1.04	0.63
Micro-Media	11,984	33,000	3.15	0.69	0.39
AMS	80,000		3.71	0.23	0.20

TABLE 10. System comparison

System	Shelf life of GPS panels (mo)	Beta-lactamase test	Custom-designed panels	Minimum order no. of panels)	Type of panel
MS-2	12	No	Yes	None	Cartridge disk
Sceptor	12	Yes	Yes	10,000	Air-dried micro-dilution tray
Micro-Media	5–6	No	Yes	1,800	Frozen micro-dilution tray
AMS	4	Yes	Yes	5,000	Air-dried card

detected >95% (6, 12) and 90% (4, 10) of the MRSA. It is current practice to regard oxacillin-resistant staphylococci as resistant to the cephalosporins, and the AMS and the other systems state this clearly. Because the AMS would require a large capital outlay, it might be suitable for the large laboratory. It was versatile in that it could accommodate a variety of cards, including those for gram-negative identification and susceptibility, gram-positive identification and susceptibility, yeast identification, enteric pathogens screen and urine screen (2, 7, 13, 15, 16). The AMS card required a more involved setup. Once learned, however, the operation of the AMS was faster than that of the other systems. The system had an efficient fault-detection mechanism, and the few mechanical problems that developed were generally simple to rectify and were attributable to inexperienced operators. Daily maintenance involved checking the incubator temperature and biweekly cleaning of the photo arrays (2 min).

The Sceptor, Micro-Media, and AMS systems performed well with a few exceptions. A major consideration in choosing one system over another should be the volume of work to be performed. The Micro-Media and Sceptor systems were suitable for the small laboratory performing 20 to 30 susceptibility tests and identifications per day, provided the Micro-Media system could detect *S. aureus* isolates that are marginally resistant to methicillin. It was easier to read the Sceptor panel than the Micro-Media panel. Although the MS-2 and AMS are not true MIC systems (results are calculated from growth curve analysis), the presence of three dilutions on the AMS MIC cards for most antimicrobial agents compared with one MS-2 disk provided a more accurate analysis of results, especially for the gram-negative organisms where growth curve susceptibility results can vary from organism to organism. Because of versatility and the reproducibility and accuracy of the GPS test results, we concluded that the AMS most closely matched our requirements.

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