Comparison of antibiotic susceptibility results obtained with Adatab* and disc methods

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SUMMARY Strains of *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, faecal streptococci, *Proteus* spp, and *Klebsiella* spp were distributed on two occasions to two groups of laboratories, one using a commercially produced break point method (Adatab, Mast Laboratories Ltd) and the other using a disc method for susceptibility testing. Minimum inhibitory concentrations of a range of antibiotics were determined for each of the strains in the Division of Microbiological Reagents and Quality Control and a correct result of sensitive or resistant was assigned where possible to each combination of strain and antibiotic. Laboratories were asked to determine the susceptibility of the strains to those antibiotics that they would test in routine practice. Results from each laboratory were compared with the correct results.

The overall error rates obtained with the Adatab and disc methods, 8% and 8.2% respectively, were not significantly different. Fewer errors were made with trimethoprim, ticarcillin, and nitrofurantoin by laboratories using Adatabs than those using discs. Fewer errors were made with gentamicin by laboratories using discs than those using Adatabs. There was no significant difference between the two groups of laboratories in reproducibility of results on repeated testing of the same strains. Laboratories using Adatabs used a wide range of different break point concentrations. The Adatab method appeared to offer no overall advantages in terms of reduced error rates or increased reproducibility of results with the strains tested.

In contrast to the United States of America, where the Kirby-Bauer method of susceptibility testing is the recommended method and is widely used, there is no standard method in the United Kingdom. Stokes' method,¹ where controls are incubated on the same plate as the test strain, and the comparative method, where controls are on a separate plate, are the most widely used methods in the UK. Considerable variations on these basic methods have been introduced by laboratories using them,² and there is no formal mechanism for updating the methods as new antibiotics are introduced. Previous trials, in which most of the participants have used disc methods, have shown high error rates associated with some combinations of organism and antibiotic.^{2,3} Although in some cases association between high error rates and certain details of

methodology could be shown, we were unable to find differences in error rates between any one of the three major methods of disc testing: Stokes' method, the comparative method, and Kirby-Bauer type methods.^{2,3}

Against this background, the introduction of the Adatab method by Mast Laboratories Ltd seemed interesting. In this method, tablets of a material containing antibiotics (supplied by the manufacturer) are dissolved in molten media, which is poured into petri dishes. The resulting plates contain a known concentration of antibiotic, which can be adjusted by altering the number of tablets added to a given volume of medium. Suspensions of organisms are then applied to the surface of the agar, usually with a multipoint inoculator, and incubated. Resistance or sensitivity is judged by growth or absence of growth on one or more concentrations of antibiotic. Since this method appears to be free of many of the potential problems associated with discs and is similar to minimum inhibitory concentration (MIC) methods,

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* Adatab is a trade mark of Mast Laboratories Ltd.

which are the reference method of testing, it would seem to be promising. In order to evaluate the method under field conditions a trial was organised, in which results from laboratories using break point methods were compared with those of laboratories using discs.

Material and methods

LABORATORIES PARTICIPATING

All laboratories included in the trial were UK clinical laboratories participating in the bacteriology section of the UK National External Microbiological Quality Assessment Scheme. Laboratories were identified as using the Adatab method from questionnaires distributed as part of a previous survey.³ For each of these laboratories, a laboratory using disc methods and which was of a similar level of performance in the previous 12 month period of the bacteriology quality assessment scheme was selected as a control. This matching of performance of the two groups of laboratories was designed to ensure that differences in results between the two groups could be attributed to the method used rather than to differences in technical skill. Twenty laboratories using the Adatab method and 24 laboratories using disc methods were included in the trial, the difference in numbers between the two groups being the result of some laboratories being unable to participate.

ORGANISMS

Five strains each of *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and faecal streptococci, all described as being from sites other than urine, and five strains each of *E. coli*, *Proteus* spp, and *Klebsiella* spp, described as isolated from urine, were distributed. Two distributions of three cultures from each of the above groups of bacteria were made with two months between distributions. One culture in each group in the second distribution was a repeat of one included in the first distribution. The strains were selected randomly from the Division of Microbiological Reagents and Quality Control culture collection. Minimum inhibitory concentrations for these strains have been determined on several occasions in the Division, and these were repeated immediately before and during the trial by the method described previously.² One strain of *Klebsiella* sp showed some contradictory results on retesting, and one strain of *S. aureus* was later found to be coagulase negative. The results from both these strains were discarded. The MICs of the remaining strains are shown in Table 1.

ANTIBIOTICS TESTED

Report forms listing for each group of organisms the appropriate set of antibiotics (as shown in Table 1) were supplied to participants, who were asked to test only those antibiotics on the list that they would normally test in routine practice. Participants were told that the trial was intended to compare the results of methods rather than to evaluate individual laboratory performance and were asked not to examine the strains more than once except in cases of gross technical failure.

ASSESSMENT OF RESULTS

Where possible a "correct" result of sensitive or resistant was assigned to each strain for each antibiotic tested. These "correct" results were derived by comparing the MICs of each strain with various published values for breakpoints.⁴⁻⁹ In cases where there was lack of agreement between published values the majority values were used. Correct results were not assigned where strains could not clearly be designated as sensitive or resistant to antibiotic on the basis of MIC results. Penicillinase producing strains of *S. aureus* were designated as resistant to penicillin regardless of the MIC. Table 1 shows the classification of the strains as sensitive or resistant. The report forms used allowed the reporting of each strain by participants as sensitive, intermediate, or resistant to each antibiotic tested. Participants' results of sensitive or resistant were regarded as correct when in agreement with the designated correct result. Discrepant results were designated as follows: minor where the reported result was intermediate and the correct result was sensitive or resistant; major where the reported result was resistant and the correct result was sensitive; and very major where the reported result was sensitive and the correct result was resistant.

Results

NUMBER OF RESULTS RETURNED

As laboratories tested only those antibiotics that they would test in routine practice, the number of reports is different for each combination of strain and antibiotic (Table 2). The difference in the number of reports received from laboratories using break points and those using discs is shown in Table 2 and reflects the fact that laboratories using discs tested a wider range of the suggested antibiotics for each organism than laboratories using Adatabs. Laboratories using Adatabs were also more restricted in the range of organisms tested—for example, some laboratories did not test urinary isolates by this method and others tested urinary isolates only.

Table 1 Minimum inhibitory concentrations (MICs) of antibiotics for the strains distributed

Organism	Antibiotic	MICs of strains designated as sensitive	MICs of strains designated as resistant	MICs of strains for which no correct result was designated*
<i>Staphylococcus aureus</i> (site other than urine)	Methicillin	0.5-2, 1-2	16-64, 8-64, 16-64	
	Tetracycline	0.25-0.5, 0.25	128, 64, 128	
	Fusidic acid	0.06-0.25, 0.06-0.25, 0.06-0.25, 0.06-0.25	4-8	
	Erythromycin	0.25-1	>128, 4-16, † 4-8, † >128	
	Penicillin		0.06-0.25, ‡ 16-32, ‡ 16-32, ‡ 0.25-4, ‡ 8-32	
<i>Pseudomonas aeruginosa</i> (site other than urine)	Gentamicin	0.1-0.5, 0.1-0.25	8-64, 16-64, 8-64	
	Gentamicin	0.5, 0.5-2, 0.5-1, 0.5-2, 0.5-1	64->128	
	Amikacin	1-4, 0.25-2, 1, 2-4, 1		4-16
	Ticarcillin	16, 32-64, 16-32, 32-64, 32, 16-32		
	Tobramycin	0.25-1, 0.1-0.25, 0.25-0.5, 0.1-0.25	64-128	2-4
<i>Klebsiella</i> spp (from urine)	Nitrofurantoin	16, 16		8-32, 16-32, 32-64
	Trimethoprim	0.5-1, 0.5-1	8-16, 8-32, 8-32	
	Sulphonamide	8-16		16-32, 16-32, 16-32, 16-32
	Cephalexin	4, 4-16, 4-16, 4-8, 4-16		
	Gentamicin	0.06-1, 0.25-0.5, 0.1-1, 0.1-1, 0.25-1	>128, 64-128, 64->128, 64->128, 32-64	
<i>Escherichia coli</i> (from urine)	Ampicillin			
	Nalidixic acid	4-8, 4-16, 4-8, 4-8, 4-8		
	Nitrofurantoin	8, 8-16, 8, 4, 8-16, 8		
	Trimethoprim	0.25-0.5, 0.1-0.25, 0.1-0.25, 0.25-0.5, 1, 0.25-0.5		
	Sulphonamide	2-4, 4-8, 8, 4-16	>512, >512	
<i>Proteus</i> spp (from urine)	Cephalexin	4-8, 2-4, 2-4, 4, 4-8, 4-8		
	Gentamicin	0.25-1, 0.25-1, 0.5-1, 0.25-1, 0.25-1, 0.5-1		
	Ampicillin	2-4, 2-4, 2-4	>128-512, 64->128, >128-512	
	Nalidixic acid	2-4, 2-4, 2-4, 4, 2-8, 2-4		
	Trimethoprim	0.5-2, 0.5, 0.5-2, 0.5-1, 1-2, 0.5		
<i>Escherichia coli</i> (site other than urine)	Sulphonamide	1, 2-4, 2, 2-4	>512, >512	
	Cephalexin	8-16, 8-16, 8, 8	32-64, 32-64	
	Gentamicin	0.1-0.25, 0.25-0.5, 0.5-1, 1, 0.5-1, 0.25-0.5		
	Ampicillin	0.5-4, 2, 2	>128, >128, >128	
	Nalidixic acid	8, 2-4, 8, 8, 8, 2-4		
<i>Faecal streptococci</i> (site other than urine)	Tetracycline	1-4, 1-4, 2, 1, 1-4	128->128	
	Trimethoprim	0.25-0.5, 0.1-0.25, 0.1-0.25, 0.25, 1, 0.1-0.25		
	Sulphonamide	2-4, 4-8, 4-8, 4-16, 4-8	>512	
	Cefuroxime	4, 2-4, 2-4, 2, 2-4, 2-4		
	Gentamicin	0.25-1, 0.25-1, 0.5-1, 0.25-1, 0.25-1, 0.5-1		
<i>Faecal streptococci</i> (site other than urine)	Ampicillin	2-4, 2-4, 2-4	>128, 64->128, 64->128	
	Tetracycline	2, 1, 0.5-2, 0.5-2	64, 64	
	Trimethoprim	0.25-1, 0.5, 0.25-1, 0.5, 0.5, 0.25-1		
	Sulphonamide		>512, >512, >512, >512, >512, >512	
	Cefuroxime	2, 2	64, 64-128, 64-128	4-8
	Ampicillin	1, 1, 0.5-1, 1-2, 1-2, 0.5-1		

Where MICs differed on repeat testing, the range of MIC values obtained is shown.

* Correct results were not designated where intermediate MIC values were obtained.

† These strains showed dissociated resistance to erythromycin.

‡ These strains were penicillinase producers.

DISCREPANCY RATES

The numbers of correct and incorrect results achieved by each group of laboratories are shown in Tables 2 and 3. There was no significant difference in the total error rate achieved by the two groups of laboratories (176 (8%) incorrect results and 2021

correct results from the laboratories using Adatabs, and 382 (8.2%) incorrect results and 4271 correct results from those using discs). Significantly more very major errors were made by laboratories using Adatabs (44 (2%) very major errors and 2153 other results from laboratories using Adatabs, and 45

Table 2 Comparison of the number of errors made by laboratories using the Adatab or disc method

Antibiotic	Adatab					Disc				
	No of errors made					No of errors made				
	None	Very major	Major	Minor	Total errors	None	Very major	Major	Minor	Total errors
<i>Staphylococcus aureus</i> (site other than urine)										
Methicillin	62	4 (6%)	2 (3%)	0	6 (9%)	113	4 (3%)	1 (1%)	2 (2%)	7 (6%)
Tetracycline	43	0	1 (2%)	0	1 (2%)	121	1 (1%)	0	1 (1%)	2 (2%)
Fusidic acid	43	1 (2%)	0	0	1 (2%)	120	2 (2%)	0	2 (2%)	4 (3%)
Erythromycin	77	0	1 (1%)	2 (3%)	3 (4%)	131	2 (2%)	0	0	2 (2%)
Penicillin	62	8 (11%)	0	1 (1%)	9 (13%)	124	7 (5%)	0	2 (2%)	9 (7%)
Gentamicin	61	0	1 (2%)	0	1 (2%)	111	0	0	1 (1%)	1 (1%)
<i>Pseudomonas aeruginosa</i> (site other than urine)										
Gentamicin	77	0	2 (2%)	5 (6%)	7 (8%)	135	0	0	0	0
Amikacin	15	0	0	0	0	102	0	1 (1%)	2 (2%)	3 (3%)
Ticarcillin	21	0	0	0	0	90	0	7 (6%)	14 (13%)	21 (19%)
Tobramycin	20	0	0	0	0	112	0	0	0	0
<i>Klebsiella</i> spp (from urine)										
Nitrofurantoin	19	0	2 (9%)	1 (5%)	3 (14%)	23	0	10 (23%)	10 (23%)	20 (47%)
Trimethoprim	43	6 (11%)	1 (2%)	6 (11%)	13 (23%)	85	2 (2%)	1 (1%)	12 (12%)	15 (15%)
Sulphonamide	3	0	8 (67%)	1 (8%)	9 (75%)	15	0	5 (24%)	1 (5%)	6 (29%)
Cephalexin	25	0	2 (7%)	1 (4%)	3 (11%)	89	0	0	0	0
Gentamicin	52	0	1 (2%)	0	1 (2%)	90	0	0	2	2 (2%)
Ampicillin	63	7 (10%)	0	1 (1%)	8 (11%)	109	1 (1%)	0	3 (3%)	4 (4%)
Nalidixic acid	47	0	9 (16%)	0	9 (16%)	95	0	3 (3%)	9 (8%)	12 (11%)
<i>Escherichia coli</i> (from urine)										
Nitrofurantoin	65	0	1 (2%)	0	1 (2%)	121	0	4 (3%)	4 (3%)	8 (6%)
Trimethoprim	65	0	1 (2%)	0	1 (2%)	117	0	0	3 (3%)	3 (3%)
Sulphonamide	64	1 (2%)	1 (2%)	0	2 (3%)	124	0	0	2 (2%)	2 (2%)
Cephalexin	28	0	2 (7%)	0	2 (7%)	102	0	0	6 (6%)	6 (6%)
Gentamicin	61	0	2 (3%)	0	2 (3%)	109	0	0	2 (2%)	2 (2%)
Ampicillin	77	1 (1%)	1 (1%)	3 (4%)	5 (6%)	132	1 (1%)	1 (1%)	1 (1%)	3 (2%)
Nalidixic acid	64	0	2 (3%)	0	2 (3%)	129	0	0	0	0
<i>Proteus</i> spp (from urine)										
Trimethoprim	63	0	3 (5%)	0	3 (5%)	92	0	8 (7%)	18 (15%)	26 (22%)
Sulphonamide	62	1 (2%)	3 (5%)	0	4 (6%)	117	1 (1%)	4 (3%)	3 (2%)	8 (6%)
Cephalexin	26	4 (12%)	1 (3%)	2 (6%)	7 (21%)	83	7 (6%)	3 (3%)	15 (14%)	25 (23%)
Gentamicin	23	0	0	0	0	111	0	0	0	0
Ampicillin	76	7 (8%)	0	0	7 (8%)	123	7 (5%)	1 (1%)	4 (3%)	12 (9%)
Nalidixic acid	62	0	0	0	0	122	0	2 (2%)	5 (4%)	7 (5%)
<i>Escherichia coli</i> (site other than urine)										
Sulphonamide	39	0	2 (4%)	4 (9%)	6 (13%)	91	0	9 (8%)	9 (8%)	18 (17%)
Trimethoprim	50	0	1 (2%)	0	1 (2%)	107	0	2 (2%)	2 (2%)	4 (4%)
Tetracycline	21	0	0	3 (13%)	3 (13%)	108	0	4 (3%)	13 (10%)	17 (14%)
Gentamicin	81	0	2 (2%)	1 (1%)	3 (4%)	132	0	0	0	0
Ampicillin	61	0	6 (8%)	11 (14%)	17 (22%)	111	0	16 (12%)	7 (5%)	23 (17%)
Cefuroxime	56	0	4 (6%)	2 (3%)	6 (10%)	102	0	3 (3%)	9 (8%)	12 (11%)
<i>Streptococcus faecalis</i> (site other than urine)										
Sulphonamide	40	2 (5%)	0	0	2 (5%)	107	4 (4%)	0	0	4 (4%)
Trimethoprim	33	0	5 (11%)	9 (19%)	14 (30%)	50	0	42 (38%)	18 (16%)	60 (55%)
Tetracycline	29	0	1 (3%)	0	1 (3%)	126	0	0	4 (3%)	4 (3%)
Ampicillin	66	0	8 (11%)	0	8 (11%)	120	0	3 (2%)	10 (2%)	13 (10%)
Cefuroxime	36	2 (5%)	0	3 (7%)	5 (12%)	70	6 (7%)	0	11 (13%)	17 (20%)
Totals	2021	44 (2%)	76 (3%)	56 (3%)	176 (8%)	4271	45 (1%)	130 (3%)	207 (4%)	382 (8.2%)

(1%) very major errors and 4608 other results from those using discs ($\chi^2 = 12.48$, $p < 0.001$).

There were apparent differences in error rates between the two groups of laboratories with the summed results for some of the antibiotics. Fewer errors were made by laboratories using Adatabs than those using discs with ticarcillin (0 incorrect results and 21 correct results from laboratories using Adatabs and 21 (19%) incorrect results and 90 correct results from those using discs, ($\chi^2 = 4.72$, $p < 0.05$)), nitrofurantoin (4 (5%) incorrect results and 84 correct results from laboratories using Adatabs

and 28 (16%) incorrect results and 144 correct results from those using discs, ($\chi^2 = 7.43$, $p < 0.01$)) and trimethoprim (32 (11%) incorrect results and 254 correct results from laboratories using Adatabs and 108 (19%) incorrect results and 451 correct results from those using discs, ($\chi^2 = 9.05$, $p < 0.01$)). In contrast, fewer errors were made by laboratories using discs than those using Adatabs with gentamicin (5 (1%) incorrect results and 688 correct results from laboratories using discs, and 14 (3%) incorrect results and 395 correct results from those using Adatabs, ($\chi^2 = 11.07$, $p < 0.001$)).

Table 3 Comparison of total errors made with individual antibiotics by laboratories using the Adatab or disc method

Antibiotic	Method	No of discrepancies					Comparison of total discrepancies
		None	Very major	Major	Minor	Total errors	
Methicillin	Adatab	62	4 (6%)	2 (3%)	0	6 (9%)	χ^2 0.60
	Disc	113	4 (3%)	1 (1%)	2 (2%)	7 (6%)	NS
Tetracycline	Adatab	93	0	2 (2%)	3 (3%)	5 (5%)	χ^2 0.14
	Disc	355	1 (<1%)	4 (1%)	18 (5%)	23 (6%)	NS
Fusidic acid	Adatab	43	1 (2%)	0	0	1 (2%)	χ^2 0.10
	Disc	120	2 (2%)	0	2 (2%)	4 (3%)	NS
Erythromycin	Adatab	77	0	1 (1%)	2 (3%)	3 (4%)	χ^2 1.09
	Disc	131	2 (2%)	0	0	2 (2%)	NS
Penicillin	Adatab	62	8 (11%)	0	1 (1%)	9 (13%)	χ^2 2.01
	Disc	124	7 (5%)	0	2 (2%)	9 (7%)	NS
Gentamicin	Adatab	395	0	8 (2%)	6 (1%)	14 (3%)	χ^2 11.07
	Disc	688	0	0	5 (1%)	5 (1%)	p < 0.001
Amikacin	Adatab	15	0	0	0	0	χ^2 0.44
	Disc	102	0	1 (1%)	2 (2%)	3 (3%)	NS
Ticarcillin	Adatab	21	0	0	0	0	χ^2 4.72
	Disc	90	0	7 (6%)	14 (13%)	21 (19%)	p < 0.05
Tobramycin	Adatab	20	0	0	0	0	—
	Disc	112	0	0	0	0	—
Nitrofurantoin	Adatab	84	0	3 (3%)	1 (1%)	4 (5%)	χ^2 7.43
	Disc	144	0	14 (8%)	14 (8%)	28 (16%)	p < 0.01
Trimethoprim	Adatab	254	6 (2%)	11 (4%)	15 (5%)	32 (11%)	χ^2 9.05
	Disc	451	2 (<1%)	53 (9%)	53 (9%)	108 (19%)	p < 0.01
Sulphonamide	Adatab	208	4 (2%)	14 (6%)	5 (2%)	23 (10%)	χ^2 1.01
	Disc	454	5 (1%)	18 (4%)	15 (3%)	38 (8%)	NS
Cephalexin	Adatab	79	4 (4%)	5 (5%)	3 (3%)	12 (13%)	χ^2 0.66
	Disc	274	7 (2%)	3 (1%)	21 (7%)	31 (10%)	NS
Ampicillin	Adatab	343	15 (4%)	15 (4%)	15 (4%)	45 (12%)	χ^2 2.75
	Disc	595	9 (1%)	21 (3%)	25 (4%)	55 (8%)	NS
Nalidixic acid	Adatab	173	0	11 (6%)	0	11 (6%)	χ^2 0.14
	Disc	346	0	5 (1%)	14 (4%)	19 (5%)	NS
Cefuroxime	Adatab	92	2 (2%)	4 (4%)	5 (5%)	11 (11%)	χ^2 0.84
	Disc	172	6 (3%)	3 (1%)	20 (10%)	29 (14%)	NS
Totals	Adatab	2021	44 (2%)	76 (3%)	56 (3%)	176 (8%)	χ^2 0.08
	Disc	4271	45 (1%)	130 (3%)	207 (4%)	382 (8.2%)	NS

REPRODUCIBILITY OF RESULTS

One each of the strains from the seven groups of bacteria was sent to participants on two separate occasions, identified on each occasion by separate strain numbers. The results of these repeated tests are shown in Table 4. Only with nitrofurantoin were there significant differences in reproducibility between the two methods: with the Adatab method 15

results were the same on both occasions of testing and no results were different and by the disc method 29 results were the same and nine results different on the two occasions of testing ($\chi^2 = 4.28$, p < 0.01). The ratio of the total number of results for all antibiotics which were the same and the total number which were different on the two occasions of testing did not differ significantly between the two

Table 4 Reproducibility on testing the seven strains distributed on two occasions

	Adatab		Disc	
	No of same results on each occasion of testing	No of different results on each occasion of testing	No of same results on each occasion of testing	No of different results on each occasion of testing
Methicillin	7	2 (22%)	14	4 (22%)
Tetracycline	12	0	50	6 (11%)
Fusidic acid	6	0	18	0
Erythromycin	11	0	20	0
Penicillin	10	0	20	0
Gentamicin	50	5 (9%)	116	4 (3%)
Amikacin	2	0	19	0
Ticarcillin	3	0	16	1 (6%)
Tobramycin	3	0	21	0
Nitrofurantoin	15	0	29	9 (24%)
Trimethoprim	32	6 (16%)	63	21 (25%)
Sulphonamide	29	3 (9%)	77	10 (11%)
Cephalexin	10	2 (17%)	40	11 (22%)
Ampicillin	47	3 (6%)	92	13 (12%)
Nalidixic acid	19	3 (14%)	50	6 (11%)
Cefuroxime	11	1 (8%)	29	3 (9%)
Total	267	25 (8.6%)	674	88 (11.5%)

methods (267 the same and 25 (8.6%) different by the Adatab method and 674 the same and 88 (11.5%) different by the disc method, $\chi^2 = 1.97$, NS).

ANTIBIOTIC CONCENTRATIONS USED IN THE ADATAB METHOD

The numbers of laboratories using various concentrations of antibiotics in the Adatab method are shown in Table 5. There were wide variations in the concentrations used for most antibiotics.

Discussion

A number of problems are inherent in this type of trial and caution is needed in interpreting the results. A particularly difficult area is the designation of "correct" results. We have, along with others, used MIC values to predict the effect of treatment, but it must be remembered that there is no absolute relation between the two. The MIC of an antibiotic for a particular organism is not an absolute value and may be influenced by such factors as inoculum density and composition of culture medium.¹⁰ A further complicating factor is the number of different break points used by various authorities⁴⁻⁹ and indeed by the participants using Adatabs in this trial. The MICs of the antibiotics used in this trial are in most cases unequivocal—that is, they would be interpreted as indicating resistance or susceptibility by a consensus of informed opinion. A few MICs would not be universally accepted as indicating susceptibility or resistance. In most of these cases a correct result has not been designated. In the remaining cases differences from the "correct" results may be due to differences in interpretation rather than to technical failure.

It is unfortunate that the number of results from the control group—that is, laboratories using discs—greatly exceeded the number from laboratories using Adatabs. The purpose of the trial was to compare results from the two methods of testing in normal routine use. For this reason laboratories were presented with a list of antibiotics for each group of bacteria and asked to test only those that they would normally test in routine practice. Laboratories using discs generally tested a larger number of antibiotics for each group of bacteria and also tested all groups of bacteria. Those using Adatabs tended to test fewer antibiotics from those on the lists and also some apparently restricted the use of Adatabs to selected groups of bacteria—for example, those from urine.

A further limitation of this trial was that the bacteria selected were all non-fastidious. Organisms such as *Neisseria gonorrhoeae* and *Haemophilus influenzae* would provide a different challenge to the two methods, but were not included as the selection of organisms was made from those likely to be tested routinely by both groups of laboratories.

The overall error rates for the two methods (8% for Adatabs and 8.2% for discs) are comparable to the overall error rates for all methods of 5.9% and 7.1% found in two previous trials of sensitivity testing methods.^{2,3} Although there was no difference in overall error rates between the two methods, more very major errors were made by laboratories using the Adatab method. Fewer errors were made by those using Adatabs for ticarcillin, nitrofurantoin, and trimethoprim than those using discs. Fewer errors were made by those using discs for gentamicin than those using Adatabs. None of the differences in error rates with other antibiotics were significant. High error rates for trimethoprim and carbenicillin

Table 5 Numbers of laboratories using various break point concentrations ($\mu\text{g/ml}$) of antibiotics

<i>Staphylococcus aureus</i> (site other than urine)									
Methicillin	4 (8)	5 (1)	8 (2)	4,8 (1)	4,10 (1)	Tetracycline	1 (3)	2 (1)	4 (1)
Fusidic acid	0.25 (1)	2 (6)	2,8 (1)	Erythromycin	0.25 (5)	0.5 (3)	1 (2)	2.5 (1)	0.25,1 (4)
Penicillin	0.06 (2)	0.25 (3)	1 (1)	2 (1)	2.5 (1)	0.015,0.06,0.25 (1)	0.06,0.25 (2)	0.25,2 (3)	
Gentamicin	1 (4)	4 (3)	1,4 (1)	1,8 (3)	2,8 (2)				
<i>Pseudomonas aeruginosa</i> (site other than urine)									
Gentamicin	4 (2)	0.5,1 (1)	0.5,2 (1)	1,2 (1)	1,4 (5)	1,8 (4)	2,8 (3)	2,4,8 (2)	
Amikacin	4 (1)	4,16 (1)	8,32 (1)	16,32 (1)	Ticarcillin	64 (1)	16,32 (1)	16,64 (1)	32,128 (2)
Tobramycin	2 (1)	0.5,2 (1)	2,8 (3)						
<i>Escherichia coli</i> (site other than urine)									
Sulphonamide	8 (3)	16 (1)	24 (1)	64 (1)	8,32 (4)	50,150 (1)	Trimethoprim	0.5 (2)	1 (2)
Tetracycline	1 (1)	4 (2)	1,4 (1)	1,4,16 (1)	Gentamicin	1 (1)	4 (2)	1,2 (1)	1,4 (5)
Ampicillin	2 (1)	4 (1)	8 (3)	1,8 (7)	2,8 (1)	2,32 (1)	8,32 (1)	1,8 (3)	2,8 (2)
Cefuroxime	2 (1)	4 (1)	8 (2)	2,8 (2)	4,8 (2)	4,16 (1)	8,32 (3)	2,4,8 (1)	
<i>Faecal streptococci</i> (site other than urine)									
Sulphonamide	8 (3)	24 (1)	64 (1)	8,32 (4)	50,150 (1)	Trimethoprim	0.5 (3)	1 (2)	4 (2)
Tetracycline	1 (1)	4 (2)	1,4 (2)	1,4,16 (1)	Gentamicin	1 (2)	4 (2)	1,2 (1)	1,8 (4)
Ampicillin	2 (1)	4 (1)	8 (2)	1,8 (7)	2,8 (3)	2,32 (1)	8,32 (1)	2,8 (3)	4,1 (3)
Cefuroxime	2 (1)	4 (2)	8 (2)	2,8 (3)	4,16 (1)	8,32 (3)		2,4,8 (1)	
<i>Escherichia coli</i> , <i>Proteus</i> spp., <i>Klebsiella</i> spp (from urine)									
Nitrofurantoin	32 (13)	16,32 (1)	Trimethoprim	4 (2)	8 (4)	16 (1)	2,8 (7)		
Sulphonamide	24 (1)	32 (6)	64 (1)	100 (1)	1000 (1)	8,32 (3)	32,12-8 (1)	50,150 (1)	
Cephalexin	32 (5)	8,16 (1)	8,32 (2)	Gentamicin	1 (1)	4 (2)	8 (3)	1,8 (4)	2,4 (1)
Ampicillin	4 (1)	8 (1)	32 (9)	1,8 (1)	2,32 (1)	8,32 (5)	Nalidixic acid	16 (1)	32 (13)

Numbers of laboratories in parentheses.

(tested instead of ticarcillin) were found in the previous two trials.^{2,3} Nitrofurantoin was not tested. While a reduction of these error rates is useful, it is disappointing that similar reductions were not found with methicillin, cephalosporins, sulphonamide, and erythromycin, all of which were associated with high error rates in the previous trials.^{2,3}

Reproducibility of test results is a factor that needs to be considered in the evaluation of any test. The ability to produce the same result on different occasions of testing is particularly important in susceptibility testing as apparent changes in the susceptibility of a strain may cause unnecessary changes in treatment of the patient. There was no significant difference in the overall reproducibility between the two methods. The number of results available for analysis of reproducibility with single antibiotics was small and it is not possible to exclude the possibility of differences between methods with individual antibiotics.

As in many other areas of microbiology there is a lack of standardisation in susceptibility testing methods in the UK. Although a particular method may be widely used, variations are introduced by individual laboratories—for example, a wide range of different disc contents is used with Stokes' method.² The Adatab method is no exception to this expression of individuality, and already a range of different concentrations of antibiotics has been introduced. Three major methods of disc testing are used: Kirby-Bauer type methods, where susceptibility is defined by strictly defined cut off points related to zone size; Stokes' method, where susceptibility is defined by comparison of test zone with the zone of a control on the same plate; and the comparative method, where sensitivity is defined by comparison of the zone size of the test strain with the zone size of a control strain on a separate plate. In contrast to the USA, where the Kirby-Bauer method is almost universally used, there is no universal method used in the UK, although Stokes' method is the single method most widely used.³ In the interests of standardisation the universal use of a single method has much to recommend it, but we have not been able to show any significant differences in error rates between these methods and have not therefore felt able to recommend the exclusive adoption of any one method.³ There are, moreover, several problems associated with disc testing¹¹ that make the use of non-disc methods such as Adatab attractive. There is no doubt, however, that it is possible to achieve a high standard of results using discs, and experience in the quality assessment scheme has shown that some laboratories consistently achieve fully correct results.^{2,3} Any method which is misused will give bad results, and this is doubtless as true of the Adatab method as it is of disc methods. It must

be emphasised that no attempt was made to optimise either the disc or Adatab methods in this trial, which was designed to compare the methods as they are performed in routine practice rather than to evaluate the potential of the methods, which can best be done in a single experienced laboratory. There would appear to be little reason to recommend changes of method unless the new method can be shown to be more reliable, and we have not shown this to be the case with the Adatab method. Other factors will influence the choice of method such as ease of use, compatibility with the routine work, and possibilities of automation, none of which we have evaluated in this trial.

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References

- ¹ Stokes EJ, Waterworth PM. Antibiotic sensitivity tests by diffusion methods. *ACP Broadsheet* 55,1972.
- ² Snell JJS, Brown DFJ, Gardner PS. An antibiotic susceptibility trial organised as part of the United Kingdom national microbiological quality assessment scheme. *J Clin Pathol* 1982;**35**:1169-76.
- ³ Snell JJS, Brown DFJ, Gardner PS. Comparison of results from two antibiotic susceptibility testing trials that formed part of the United Kingdom national external quality assessment scheme. *J Clin Pathol* 1984;**37**:321-8.
- ⁴ Waterworth PM. Laboratory Control. In: Garrod LP, Lambert HP, O'Grady F. *Antibiotic and chemotherapy*. 5th ed. Edinburgh: Churchill Livingstone, 1981;464-504.
- ⁵ Ericsson HM, Sherris JC. Antibiotic sensitivity testing. Report of an international collaborative study. *Acta Pathol Microbiol Scand [B]* 1971;**217**(suppl):1-90.
- ⁶ NCCLS subcommittee for antimicrobial susceptibility tests. *Performance standards for antimicrobial disc susceptibility tests*. 2nd ed. Lancaster Avenue, Villanova, Pa 19085, USA: National Committee for Clinical Laboratory Standards, 771E, 1979.
- ⁷ Swedish reference group for antibiotics. A revised system for antibiotic sensitivity testing. *Scand J Infect Dis* 1981;**13**:148-52.
- ⁸ DIN 58940. Methoden zur empfindlichkeitsprüfung von bakteriellen krankheitserregern (ausser mykobakterien) gegen chemotherapeutica: bewertung der minimalen hemmkonzentration. 1979: Standards Commission (Medical), German Institute for Standards, Burggraben Strasse, 4-7, 1 Berlin 30, West Germany.
- ⁹ Shannon KP, Phillips I, King BA. Aminoglycoside resistance among *Enterobacteriaceae* and *Acinetobacter* species. *J Antimicrob Chemother* 1978;**4**:131-42.
- ¹⁰ Waterworth PM. Quantitative methods for bacterial sensitivity testing. In: Reeves DS, Phillips I, Williams JD, Wise R, eds. *Laboratory methods in antimicrobial chemotherapy*. Edinburgh: Churchill Livingstone, 1978;31-40.
- ¹¹ Brown DFJ, Blowers R. Disc method of sensitivity testing and other semiquantitative methods. In: Reeves DS, Phillips I, Williams JD, Wise R, eds. *Laboratory methods in antimicrobial chemotherapy*. Edinburgh: Churchill Livingstone, 1978;8-30.

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