

Technical Notes

ADDITIONS AND MODIFICATIONS TO THE RANGE OF ANTIBIOTICS TESTED BY THE CDS METHOD OF ANTIBIOTIC SENSITIVITY TESTING

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INTRODUCTION

The Calibrated Dichotomous Sensitivity disc method of antibiotic sensitivity testing (CDS method), was described first in Pathology in 1975.¹ One requirement of the method is that with each antibiotic the disc test is calibrated to a quantitative sensitivity determined by an internationally accepted reference method.² An extended and modified list of antibiotics which have been calibrated for testing by the CDS method is provided below (Tables 1a-d). Included in the tables for each antibiotic is the potency of the disc used, the "sensitive" minimum inhibitory concentration (MIC) referred to in the calibration of the test and the mean and standard deviation of a series of measurements of the annular radii of the inhibitory zones observed with the appropriate reference strain. Details of the application and significance of this information are contained in the original and subsequent full descriptions of the CDS method.^{1,3,4}

TABLE 1a Disc content, MIC of sensitive strains and the mean and standard deviation of annular radii (mm) of the reference strain for gram positive organisms

Antibiotic and disc content (μg)	MIC of sensitive strains (mg/l)	Mean (\pm SD) of annular radii (mm) of reference strain (<i>Staph aureus</i> NCTC 6571 [Oxford])
Benzylpenicillin (1.5u)	≤ 0.06	13.2 \pm 0.7
Chloramphenicol (30)	≤ 8.0	9.6 \pm 1.2
Ciprofloxacin (2.5)	≤ 1.0	10.4 \pm 0.7
Enoxacin (10)	≤ 4.0	11.4 \pm 0.8
Erythromycin (5)	≤ 0.5	9.4 \pm 0.6
Fusidic acid (2.5)	≤ 0.5	9.9 \pm 0.9
Gentamicin (10)	≤ 1.0	8.4 \pm 0.5
Kanamycin (50)	≤ 4.0	7.4 \pm 0.6
Methicillin (10)	≤ 4.0	10.1 \pm 0.7
Nitrofurantoin* (200)	≤ 32	8.6 \pm 0.9
Rifampicin (1)	≤ 0.5	10.4 \pm 0.8
Sulphafurazole* (300)	≤ 64	11.7 \pm 1.1
Tetracycline (30)	≤ 2.0	13.1 \pm 1.3
Trimethoprim* (2.5)	≤ 2.0	6.8 \pm 0.7
Vancomycin (60)	≤ 2.0	6.1 \pm 0.5

*Used only for coagulase negative staphylococci isolated from urine.

There has been a considerable increase in the number of antibiotics which laboratories are now asked to test and to cater for this need the tables have been expanded to include all of the newer antibiotics for which the disc test was found to be an appropriate method of testing. However it is not expected that laboratories would test all the agents listed but that they would select the most suitable combination of antibiotics on the basis of their own requirements. With each of the antibiotics added to the list sensitivity is indicated by an inhibitory zone with

TABLE 1b Disc content, MIC of sensitive strains and the mean and standard deviation of annular radii (mm) of the reference strain for gram negative organisms (Enterobacteriaceae)

Antibiotic and disc content (μg)	MIC of sensitive strains (mg/l)	Mean (\pm SD) of annular radii (mm) of reference strain (<i>E. coli</i> NCTC 10418; except where indicated)
Amikacin (30)	≤ 4.0	9.0 \pm 0.7
Ampicillin (25)	≤ 8.0	10.0 \pm 0.5
Augmentin* (60) ¹	$\leq 8.0/4.0^2$	7.9 \pm 0.5 ³
Aztreonam (10)	≤ 4.0	13.6 \pm 1.0
Cefotaxime (5)	≤ 1.0	12.6 \pm 0.8
Cefotetan (10)	≤ 4.0	12.6 \pm 0.5
Cefoxitin (30)	≤ 8.0	11.7 \pm 0.5
Ceftazidime (10)	≤ 4.0	11.0 \pm 0.6
Ceftriaxone (5)	≤ 2.0	12.9 \pm 0.7
Chloramphenicol (30)	≤ 8.0	10.2 \pm 0.9
Ciprofloxacin (2.5)	≤ 1.0	13.4 \pm 0.9
Enoxacin (10)	≤ 4.0	12.8 \pm 0.6
Gentamicin (10)	≤ 1.0	9.1 \pm 0.7
Imipenem (10)	≤ 4.0	12.5 \pm 0.8
Kanamycin (50)	≤ 8.0	8.6 \pm 0.6
Latamoxef (5)	≤ 1.0	11.6 \pm 0.6
Nalidixic acid* (30)	≤ 4.0	9.7 \pm 0.5
Netilmicin (30)	≤ 2.0	10.5 \pm 0.8
Nitrofurantoin* (200)	≤ 32	8.9 \pm 0.6
Norfloxacin* (10)	≤ 4.0	13.7 \pm 0.5
Sulphafurazole (300)	≤ 64	9.1 \pm 1.5
Tetracycline (30)	≤ 4.0	8.6 \pm 0.9
Timentin (85) ⁴	$\leq 32/2.0^5$	7.2 \pm 0.7 ³
Tobramycin (10)	≤ 1.0	7.8 \pm 0.6
Trimethoprim (2.5)	≤ 2.0	10.3 \pm 1.0

*For testing urinary tract isolates only.

1. Amoxycillin 40 μg + clavulanic acid 20 μg .

2. Amoxycillin 8 mg/l + clavulanic acid 4 mg/l.

3. Reference strain *Escherichia coli* NCTC 11560.

4. Ticarcillin 75 μg + clavulanic acid 10 μg .

5. Ticarcillin 32 mg/l + clavulanic acid 2 mg/l.

TABLE 1c Disc content, MIC of sensitive strains and the mean and standard deviation of annular radii (mm) of the reference strain for *Pseudomonas aeruginosa*.

Antibiotic and disc content (μg)	MIC of sensitive strains (mg/l)	Mean (\pm SD) of annular radii (mm) of reference strain (<i>Ps. aeruginosa</i> NCTC 10662; except where indicated)
Amikacin (30)	≤ 16	8.9 ± 0.8
Aztreonam (30)	≤ 8.0	10.4 ± 0.6
Ceftazidime (10)	≤ 4.0	9.0 ± 0.7
Ciprofloxacin (2.5)	≤ 2.0	12.1 ± 1.0
Enoxacin (10)	≤ 4.0	11.3 ± 0.9
Gentamicin (10)	≤ 4.0	8.5 ± 0.8
Imipenem (10)	≤ 4.0	9.5 ± 0.8
Netilmicin (30)	≤ 8.0	8.7 ± 0.9
Piperacillin (50)	≤ 16	9.9 ± 0.6
Polymyxin (300 u)	≤ 1.0	6.2 ± 0.5
Ticarcillin (75)	≤ 32	7.9 ± 0.8
Timentin (85) ¹	$\leq 32/2.0^2$	7.2 ± 0.7^3
Tobramycin (10)	≤ 4.0	9.1 ± 0.6

1. Ticarcillin 75 μg + clavulanic acid 10 μg .
2. Ticarcillin 32 mg/l + clavulanic acid 2 mg/l.
3. Reference strain *Escherichia coli* NCTC 11560.

TABLE 1d Disc content, MIC of sensitive strains and the mean and standard deviation of annular radii (mm) of the reference strain for *Haemophilus influenzae*

Antibiotic and disc content (μg)	MIC of sensitive strains (mg/l)	Mean (\pm SD) of annular radii (mm) of reference strain (<i>H. influenzae</i> NCTC 4560)
Ampicillin (2)	≤ 1.0	7.6 ± 1.1
Chloramphenicol (10)	≤ 2.0	9.3 ± 0.8
Cefotaxime (5)	≤ 0.12	11.5 ± 1.3

an annular radius of 6 mm or more. Where the disc potency of an established antibiotic has been changed the sensitive/resistant cut-off annular radius is also maintained at 6 mm. Thus the only exceptions to the uniform 6 mm cut-off annular radius in the CDS test remain *Pseudomonas* with polymyxin and the aminoglycosides and *Staphylococcus aureus* with vancomycin where, in each case, a sensitive zone size is 4 mm or more annular radius.

Reports of erythromycin resistance in *Streptococcus pyogenes*⁵ and chloramphenicol resistance in *Haemophilus influenzae* type b⁶ necessitated a

recalibration of these two antibiotics at lower disc strengths. Erythromycin was recalibrated for all Gram positive species using a 5 μg disc instead of a 15 μg disc. The use of a 5 μg disc enabled a much greater distinction to be made between erythromycin-resistant and erythromycin-sensitive strains of *Streptococcus pyogenes* and this disc potency was also found to be satisfactory for other Gram positive species. Resistance to chloramphenicol in *Haemophilus influenzae* type b was more clearly demonstrated with a 10 μg disc than with a 30 μg disc. Consequently, discs with a 10 μg potency are now used to discriminate between resistant and sensitive strains of *Haemophilus influenzae* type b. However, discs of this potency are not suitable for tests with other organisms and the 30 μg disc of chloramphenicol is retained for testing other Gram negative and Gram positive species.

Nitrofurantoin, sulphafurazole and trimethoprim were added to those antibiotics calibrated for the Gram positive species to enable laboratories to meet requests to test the antibiotic sensitivity of coagulase-negative staphylococci associated with urinary tract infection. None of these three agents was calibrated with other Gram positive organisms and their use is restricted to testing coagulase-negative staphylococci isolated from urine.

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