

In Vitro Susceptibility of *Corynebacterium diphtheriae* to Thirteen Antibiotics

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Fourteen isolates of *Corynebacterium diphtheriae* proved to be most susceptible to erythromycin and rifampin and were also inhibited by 11 other antibiotics tested.

Diphtheria has reappeared as an important medical problem in the United States with major outbreaks occurring recently in Illinois and in Texas (5, 8). No studies of the susceptibility of *Corynebacterium diphtheriae* to multiple antibiotics have been reported in the English language since the work of Jackson and associates in 1950 (4). The present investigation was undertaken to determine the current susceptibility of freshly isolated strains of *C. diphtheriae* to the commonly employed and newer antibiotics. This was felt to be important since the development of the carrier state remains a problem (8).

Fourteen known toxin-producing strains of *C. diphtheriae* isolated in Texas during 1970 were tested for antibiotic sensitivity by a quantitative plate dilution technique. These isolates consisted of four strains from unrelated sporadic cases of diphtheria in Houston, four strains from Houston children with pharyngitis who had history of previous immunizations and negative Schick tests, and six strains which were isolated during the 1970 San Antonio epidemic.

The corynebacteria were grown in Tryptose phosphate broth for 18 hr at 37 C, which was found, by appropriate colony counts, to yield a suspension of 10^8 organisms/ml. Mueller-Hinton agar plates containing serial twofold dilutions of the various antibiotics were streaked with a 0.01-ml loop of a 10^{-1} dilution of the initial broth culture for a final inoculum of 10^5 organisms. A control strain of *Staphylococcus aureus* (FDA 209P) of known antibiotic susceptibility was also streaked onto each plate for a final inoculum of 10^5 bacteria. The minimum inhibiting concentration (MIC) was taken as the lowest antibiotic concentration allowing no growth after incubation at 37 C for 24 hr.

The results of in vitro susceptibility testing are presented in Table 1. Erythromycin and rifampin were found to be slightly more active than penicillin G on a weight basis. Ampicillin, cephalo-

thin, cephalixin, and lincomycin were approximately equal in efficacy. Cephalixin, chloramphenicol, tetracycline, gentamicin, and kanamycin were somewhat less active than the other agents tested, and oxacillin was found to be least active.

Review of the literature since 1950 reveals reported susceptibility (MIC) to antibiotics as

TABLE 1. Antibiotic susceptibility of *Corynebacterium diphtheriae*

Antibiotic	No. of strains with minimum inhibiting concn ($\mu\text{g/ml}$) of									
	0.0125	0.025	0.05	0.1	0.2	0.4	0.8	1.6	3.1	
Penicillin G			2	4	8					
Ampicillin				1	5	8				
Oxacillin								4	10	
Erythromycin	2	7	5							
Tetracycline						6	8			
Lincomycin						13	1			
Rifampin	6	5	3							
Chloramphenicol						1	4	9		
Cephapirin					9	5				
Cephalixin							7	7		
Kanamycin							2	5	7	
Gentamicin						5	8	1		
Cephalothin					5	9				

follows: penicillin, 0.2 to 0.8 $\mu\text{g/ml}$; chloramphenicol, 1.6 to 6.3 $\mu\text{g/ml}$; oxytetracycline, 0.8 to 3.1 $\mu\text{g/ml}$; erythromycin, 0.01 $\mu\text{g/ml}$; cephalothin (two strains only), 0.05 and 0.195 $\mu\text{g/ml}$, respectively; and cephalixin (two strains only) 1.25 $\mu\text{g/ml}$ (2, 3, 4, 7). The results obtained in our investigation reveal no significant changes in the susceptibility of *C. diphtheriae* to these agents.

The relatively low MIC of gentamicin against these strains noted in the present study may ex-

plain the clinical observations of Martin and White (6). These authors noted that when gentamicin was used for the reduction of staphylococci in nasal carriers there was a concomitant reduction in the isolation of diphtheroid organisms. Our studies show that rifampin is also highly active against *C. diphtheriae* in vitro. This suggests that rifampin has a potential application in treatment of the carrier state as has been noted with the use of this drug by Deal and Sanders in the management of meningococcal carriers (1).

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Antibiotic standards were supplied by the following manufacturers: Bristol Laboratories, Inc. (potassium penicillin G, ampicillin, kanamycin, tetracycline, oxacillin, and cephalirin), Eli Lilly & Co. (cephalothin, cephalixin, erythromycin), Parke, Davis & Co. (chloramphenicol), The Upjohn Co. (lincomycin), Ciba Pharmaceutical Products, Inc. (rifampin), and Schering Corp. (gentamicin).

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