effects. (1–7) These characteristics suggested that ampicillin might be an ideal single drug for the treatment of acute suppurative meningitius due to *D. pneumoniae, N. meningitidis, or H. influenzae.* The parenteral form of ampicillin was released for clinical trials in the United States in 1963. During 1963, Ivler and his associates (8) published a preliminary report of in vitro studies and clinical experiences, in the management of 31 patients with purulent meningitis due to various organisms, including *D. pneumoniae, N. meningitidis, and H. influenzae.* A more detailed report of the treatment of *H. influenzae* meningitis with ampicillin was presented at the International Conference on Therapy With the New Penicillins (9) in 1964. These investigators found that 126 strains of *H. influenzae* isolated from the cerebrospinal fluid were sensitive to ampicillin. Ninety-one per cent of the strains were killed by 0.4 mcg. per milliliter and only one strain required as much as 1.6 mcg. for bactericidal activity. Ampicillin and penicillin G were both bactericidal at 0.4 mcg. per milliliter for greater than 90 per cent of 72 strains of *N. meningitidis* and 37 of *D. pneumoniae.* Ivler, Thrupp, and co-workers (8, 9) found that ampicillin was comparable to chloramphenicol and equal to penicillin G in efficacy for the treatment of bacterial meningitis. Ampicillin did not appear to have any definite advantages over chloramphenicol other than freedom from hematologic depression.

During 1963 and 1964 similar laboratory and clinical investigations were conducted at the Texas Medical Center in Houston. This report summarizes the results of these investigations. Since the majority of the laboratory studies were performed as a base line for the clinical studies, the laboratory data are presented as Part I and the clinical studies as Part II.

PART I. LABORATORY STUDIES

In vitro sensitivity tests. Prior to the initiation of clinical studies, strains of *D. pneumoniae, N. meningitidis* group C, and *H. influenzae* Type B freshly isolated from patients with meningitis in the Houston area were tested for susceptibility to ampicillin,* tetracycline, chloramphenicol, and penicillin G. The two-fold serial tube dilution technique using tryptose phosphate broth and an inoculum of approximately 10^4 organisms was employed for the determination of the minimal bactericidal concentration (MBC) of pneumococci and meningococci. Agar diffusion plates were used in determining the minimal inhibitory concentration (MIC) of *H. influenzae.* Casman's agar base with 10 per cent heated blood was employed as the medium. The plates were inoculated from a 24 hour culture in 5 per cent blood and brain-heart infusion broth with a standard 5 mm. wire loop. All of the strains tested during the preliminary phase of investigation were sensitive in vitro to all four of these antibiotics. Since the results of sensitivity tests of organisms isolated from patients enrolled in the later clinical trials were similar to those obtained in the preliminary studies, the cumulative results are presented in Table I.

TABLE I.—MINIMAL INHIBITORY CONCENTRATIONS OF AMPICILLIN, CHLORAMPHENICOL, PENICILLIN G AND TETRACYCLINE AGAINST HEMPOHILUS INFLUENZAE AND MINIMAL BACTERICIDAL COCENTRATIONS OF THESE SAME DRUGS AGAINST DIPLOCOCCUS PNEUMONIAE ANDNEISSERIA MENINGITIDIS STRAIN: SOLATED FROM PATIENTS WITH MENINGITIS

Antibiotic	Number of strains tested	Antibiotic concentration								
		0.012 (mcg./ml.)	0.025 (mcg./ml.)	0.05 (mcg./ml.)	0.01 (mcg./ml.)	0.20 (mcg./ml.)	0.39 (mcg./ml.)	0.79 (mcg./ml.)	1.56 (mcg./ml.)	3.12 (mcg./ml.)
Hemophilus influenzae:										
Amipicillin	41		2			10	26	3		
Chloramphenicol	24					4	6	4	10	
Penicillin G	15					2	9	1	3	
Tetracycline	27					2	7	7	11	
Diplococcus pneumoniae:										
Ampicillin	12	2	6	4						
Chloramphenicol	11								3	8
Penicillin G	12		5	7						
Tetracycline	11				5	3	2		1	
Neisseria meningitidis:										
Ampicillin	15		1	8	5	1				
Chloramphenicol	7							3	4	
Penicillin G	13		1	4	7	1				
Tetracycline	7						3	4		

*Polycillin (Bristol Laboratories).