

underlying disease or complications as noted above. Because of its effectiveness and lack of toxicity, penicillin G represents the agent of choice in known meningococcal and pneumococcal infections. Penicillin, when given alone and in adequate doses, clearly provides as effective a response as sulfonamides (6). Even though sulfonamides were previously recommended for meningococcal disease, the prevalence of sulfonamide-resistant meningococci in civilian populations (33 per cent among our patients) during the last 3 years has made reliance upon these agents impossible for optimal therapy of meningococcal disease (4).

On the basis of both *in vitro* and *in vivo* data (3, 7), ampicillin is at least as effective against *H. influenzae*, Type B, as is chloramphenicol, and shares with penicillin G its bactericidal activity against both the meningococcus and pneumococcus (3). This activity, with its concomitant lack of toxicity, makes ampicillin a logical choice for initial therapy in the patient older than 2 months of age when there is no evidence suggesting that an unusual organism may be present.

Early laboratory and clinical trials with ampicillin in acute bacterial meningitis due to *H. influenzae* were begun in 1962. It was immediately apparent that ampicillin was bactericidal *in vitro* against strains of *H. influenzae*, Type B, which were isolated from spinal fluid at levels easily attainable in the patient (3). No resistant strains of the organism have been identified, although disc sensitivity tests have frequently been misleading. The disc sensitivity of *H. influenzae*, Type B, against ampicillin may suggest that the organism is resistant, but careful tube dilution tests have confirmed the uniform sensitivity of these organisms to date.

After initial *in vitro* studies of many isolates, ampicillin was administered cautiously to patients with meningitis due to *H. influenzae* who had been partially treated with chloramphenicol. After this, ampicillin was cautiously used as initial therapy in individuals not critically ill, and it seemed at least equivalent to chloramphenicol. Concomitant cautious early trials seemed to indicate that ampicillin was also at least as effective as penicillin G in the treatment of pneumococcal and meningococcal meningitis. At that time, an alternate patient study, which compared ampicillin therapy with conventional therapy as used in many hospitals throughout the world, was instituted in patients older than 2 months. The results of the initial steps in this evaluation confirmed the effectiveness of ampicillin (3, 9, 12, 13).

TABLE IV.2.—SINGLE VERSUS MULTIPLE ANTIMICROBIAL THERAPY IN ACUTE BACTERIAL MENINGITIS¹

Severity ² of illness on admission	Therapeutic regimen selected								
	Ampicillin alone			Ampicillin+chloramphenicol+streptomycin			Total patients treated		
	Cases	Deaths	Percent	Cases	Deaths	Percent	Cases	Deaths	Percent
Mild.....	88	1	1.1	67	0	-----	155	1	0.6
Moderate.....	13	0	-----	9	0	-----	22	0	0
Severe.....	28	4	14.3	35	13	37.2	63	17	27.0
Total.....	129	5	3.9	111	13	11.7	240	18	7.5

¹ Patients excluded: infants <2 months of age, 15; unusual organisms, 15; error in treatment assignment, 9; endocarditis, mechanical defect, etc., 6; total exclusions, 45 with 11 deaths. Table was computed by severity of illness. Los Angeles County General Hospital, 1 year experience to July 1966.

² See footnote 1 to table IV.1.