TABLE IV.3.—SINGLE VERSUS MULTIPLE ANTIMICROBIAL THERAPY IN ACUTE BACTERIAL MENINGITIS [1]

Age group of patients	Therapeutic regimen selected					
	Ampicillin alone		Ampicillin+ chloramphenicol+ streptomycin		Total patients treated [2]	
	Cases	Deaths	Cases	Deaths	Cases	Deaths
2 to 11 months	35	1	25	2	60	3
1 to 14 years	57	0	49	1	106	1
15 to 44 years	16	0	19	1	35	1
45 to 59 years	15	4	8	3	23	7
60-plus years	6	0	10	6	16	6
Total	129	5	111	13	240	18
Case fatality (percent)	3.9		11.7		7.5	

[1] Table computed by age group of patients. Los Angeles County General Hospital, 1-year experience to July 1966.
[2] Patients excluded: infants >2 months of age, 15; unusual organisms, 15; error in treatment assignment, 9; endocarditis, mechanical defect. 6; total exclusions, 45 with 11 deaths.

Additional data from our most recent study of the treatment of meningitis in patients older than 2 months of age are shown in Tables IV.2, IV.3, and IV.4. Therapy consisted of ampicillin alone in an initial intravenous push dose of 50 mg. per kg., followed by 150 mg. per kg. per day in six divided push doses at 4-hour intervals, and contrasted ampicillin alone with ampicillin plus two other drugs. Alternate patients received therapy consisting of a combination of the same dose of ampicillin plus chloramphenicol at 100 mg. per kg. per day, to a maximum of 4 gm. each day for the total duration of therapy, and streptomycin at 40 mg. per kg. per day (to a maximum of 2 gm.) for the initial 2 days of treatment. Administration of chloramphenicol was delayed until 30 min. after ampicillin had been administered in an effort to avoid antibiotic interference.

As noted in Table IV.2, the response to ampicillin was excellent, with only five deaths among 129 patients treated or an over-all mortality of 3.9 per cent. Multiple antibiotic treatment yielded 13 deaths among 111 patients, a mortality rate of 11.7 percent. The difference is statistically significant ($x^2=5.33$; $p=<0.02$). Although a slight chance variation is seen in that more patients with milder disease were randomly included in the ampicillin category, this shift is not sufficient to explain the difference observed.

In Table IV.3 the effect of increasing age on mortality is shown. However, it is important to note that the excess mortality seen with the multiple drug regimen included all ages and was not caused by the chance assignment of the elderly alcoholic with his associated high mortality rate to this treatment group.

When the responses of patients, in specific etiological categories, to treatment with ampicillin alone or to the multiple routine were compared (Table IV.4), no single type of infection seemed to contribute excessively to the higher mortality among the patients in the multiple drug group.

It is apparent from these data that there is no advantage, and a possible disadvantage, to using more than a single agent in the therapy of the common types of acute bacterial central nervous system infections. Whenever possible, we believe that therapy should be specific.

Acute bacterial central nervous system disease during the first 60 days of life, particularly in the newborn, represents a totally different problem. At this age, enteric organisms are much more frequently encountered, and their antimicrobial sensitivities are impossible to predict accurately. The organisms isolated from patients in our hospital with neonatal meningitis during the past 5 years are listed in Table IV.5. No single antimicrobial agent is optimally effective against more than two-thirds of these organisms, although, on the basis of *in vitro* data, a combination of either penicillin or ampicillin plus kanamycin is effective in more than 95 percent. The importance of repeated spinal fluid examinations to determine the course of the disease for guidance of therapy is extremely important at this age. Even antimicrobial agents selected on the basis of careful *in vitro* testing may be ineffective when given in the usual dosage.