RESULTS

Distribution of patients. During the period from 1 July 1963 through 30 April 1965, a total of 541 patients with bacterial meningitis were admitted to the Communicable Disease Service. The distribution of these patients by etiological agent is shown in Table 1. The 88 total exclusions comprise patients who were inadvertently assigned to the inappropriate therapeutic group (43), or were subsequently discovered to have nonpurulent meningitis (7). Those with underlying disease [brain abscess (4) or bacterial endocarditis (7)] were also excluded, as were those with dual infection (1), unusual organisms (10), and those patients known to be hypersensitive to penicillin (6). Within the meningococcal category, those considered by the admitting physician to have fulminant meningococcal disease were also excluded. Five patients who would have received ampicillin and five patients who might have been assigned to the control group were thus excluded. All received penicillin G, and two deaths occurred among these 10 patients, one in each category should they have been included.

Source of organisms. Of the 453 patients suitable for analysis, precise bacterial etiologies were determined in 368, or 81%. Although many of the patients had received at least some antibacterial therapy prior to their admission, this was not a reason for exclusion, since, despite previous antibacterial therapy, the organism was recovered on culture from the great majority of patients, as is noted in Table 2. In 32 instances, organisms were identified on direct examination of spinal fluid or petechiae without subsequent growth in culture. Twenty-one patients with purulent meningitis and a petechial-purpuric rash were included in the meningococcal category on clinical grounds.

Severity of illness. To properly categorize patients for comparative purposes, they were divided into four groups according to the severity of illness at the time of admission to the hospital. Included in the 4+ (severe) category, were patients who were comatose or semicomatose, in definite shock, or with significant hypotension. The 3+ (moderate) category included patients with convulsions, but who were not hypotensive or comatose. The 2+ (mild) category had patients in whom either the temperature was greater than 105 F rectally on admission, or symptoms had been present for more than 5 days; also included were those with a complication already present on admission or with marked lethargy. The 1+ (mild) category was reserved for those patients with none of the above findings but with definite bacterial meningitis. Since the 2+ and 1+ categories were associated with low mortality and few complications, these grades have been combined and are presented for all groups in Table 3. As is apparent, the distribution of severe and lesser grades of illness was essentially the same for the ampicillin and the control groups. The method of randomization was effective, although minor differences in proportions of patients in moderate and severe categories were seen.

In the pneumococcal severe category there was an apparent difference in the assignment of excess patients in the severe group to penicillin therapy. This difference is not statistically significant ($X^2=3.28$; $P=0.077$), and is explained by the difference in age distribution for pneumococcal cases (Table 4). Fewer control patients appear in the 1 to 15-year group, and an excess is apparent in the 30 to 44-year and 60 to 74-year groups. The slightly lower mortality in pneumococcal disease with ampicillin therapy may be explained entirely by the age and severity distributions in this study.

TABLE 3.—TYPES OF MENINGITIS BY SEVERITY ON ADMISSION

Etiology and regimen	Clinical estimate on severity						Total cases
	Severe		Moderate		Mild		
	Number	Percent	Number	Percent	Number	Percent	
Haemophilus influenzae:							
Ampicillin	13	20	10	15	43	65	66
Control therapy	18	17	20	18	69	65	107
Neisseria meningitidis:							
Ampicillin	13	23	10	18	33	59	56
Control therapy	23	30	4	5	50	65	77
Diplococcus pneumoniae:							
Ampicillin	22	54	3	7	16	39	41
Control therapy	31	74	2	5	9	21	42
Unknown:							
Ampicillin	3	10	5	17	21	73	29
Control therapy	5	14	0	0	30	86	35