Ampicillin was highly effective in vitro against *Haemophilus influenzae*, *Neisseria meningitidis*, and *Diplococcus pneumoniae*, and, being a penicillin, would be expected to have low toxicity. Therefore, ampicillin as a single drug treatment for bacterial meningitis was contrasted with "conventional" therapy. From 1 July 1963 to 30 April 1965, 541 bacterial meningitis patients over 2 months of age were assigned to ampicillin therapy or to conventional therapy with penicillin, chloramphenicol, or both, according to chart number. Error in drug assignment, fulminant meningococcemia, unusual organisms, or concomitant disease requiring other therapy excluded 88 patients. The severity of illness on admission was comparable in both treatment groups. Overall mortality rates in the ampicillin (A) and control (C) groups were 8.3 and 11.8%, respectively. Case fatality rates varied slightly according to etiological agent, i.e., *H. influenzae* (6.0 with A versus 9.3 with C); *N. meningitidis* (5.3 with A versus 9.1 with C); *D. pneumoniae* (22.0 with A versus 28.7 with C); purulent meningitis, no isolate (0 with A versus 5.7 with C). The overall incidence of neurological residua was 12.5% with A and 10.7% with C. Duration of fever and cerebrospinal fluid abnormalities were comparable. Possible complications of therapy were more frequent in the control group, primarily because of hematological changes with chloramphenicol. The data indicate that ampicillin is effective as a single drug for the three major causes of bacterial meningitis and purulent meningitis of unknown etiology, and also illustrate the difficulties inherent in naming a "regimen of choice" when two effective modes of treatment are compared.

Although serum therapy, sulfonamides, and subsequently the use of various antibiotics have substantially reduced the mortality of bacterial meningitis, the total case fatality rate remains between 10 and 15% in many large series. Current therapeutic recommendations for the most frequent types of bacterial meningitis include one or more of several different antimicrobial agents. Of the drugs most frequently recommended, only benzylpenicillin lacks major pharmacological toxicity. A new 6-amino-penicillanic acid derivative, ampicillin, demonstrated marked bactericidal activity against *Haemophilus influenzae* in vitro and resembled benzylpenicillin in potential toxicity and efficacy against organisms customarily penicillin-sensitive (Ivler et al., 1964). Therefore, it seemed desirable to evaluate this antibiotic in the therapy of *H. influenzae* and other types of acute bacterial central nervous system (CNS) infections.

After treatment of a small number of patients seemed to indicate clinical efficacy and no toxicity, a controlled clinical evaluation of parenteral ampicillin in comparison with groups treated with penicillin or chloramphenicol or both, was started at the Communicable Disease Service of the Los Angeles County General Hospital in 1963. A preliminary report of this study (Ivler et al., 1964) and some of the data concerning patients with *H. influenzae* have been presented previously (Thrupp et al., 1964).

MATERIALS AND METHODS

Selection of patients. The Communicable Disease Service of the Los Angeles County General Hospital is the major referral center for the entire County for patients with CNS infections of all ages and from all socioeconomic groups. Patients were included in the present study in accordance with the following criteria. All patients 2 months of age and older who were admitted to the Communicable Disease Service of the Los Angeles County General Hospital with bacterial meningitis were included in this study. Patients were assigned to the ampicillin or control groups on the basis of hospital chart numbers. Chart numbers were obtained by telephoning the central admitting office, which obviated physician bias in assignment of patients to one group or another. Patients with even chart numbers were assigned to the ampicillin group, and those with odd chart numbers, to the control group.

Administration of antibiotic therapy. One-third of the 24-hr dose of the respective antibiotic was given by rapid intravenous infusion on admission to the service. Sodium ampicillin was given in a daily dose of 150 mg/kg, intravenously, in equally divided doses at 4-hr intervals. Each dose of ampicillin was dissolved in 0.85% sodium chloride and was administered as a rapid infusion. Reconstituted drug was stored in a refrigerator at 4 C for not more than a 24-hr period. After a minimum of 2 or 3 days of intravenous therapy, the antibiotic was given intramuscularly, at the same dosage, on a 4-hr schedule. Control therapy consisted of penicillin G in doses approximating 150 mg/kg for patients with

NOTE.—References at end of article.