

No attempt was made to evaluate this, since it was assumed to provide an equal, and probably negligible, effect in both treatment groups.

(2) Administration of antibacterial therapy: Sodium ampicillin was reconstituted in 0.85 per cent NaCl and administered rapidly (15–20 minutes) at four hour intervals in a total daily dose of 150 mg./kg. of body weight. (The first seven patients treated received 100 mg./kg. per day intravenously at six hour intervals). The intravenous route was used invariably for at least the first 48 hours, while after adequate initial clinical response many patients were given the same daily dose by intramuscular injection at four hour intervals during the remainder of the period of treatment.

Chloramphenicol was given by continuous intravenous infusion in a total daily dose of 100 mg./kg. In some patients in whom the diagnosis of *H. influenzae* was not certain on admission, sulfisoxazole and penicillin G (150 mg./kg./day of each drug) were also given until isolation and identification of the organisms were completed.

(3) Duration of therapy: Treatment was continued until the patient was afebrile for at least five days, the spinal fluid contained less than 40 cells per cmm. with few or no polymorphonuclear leukocytes, and the C.S.F. sugar was normal.

(4) Evaluation of response to therapy: Response to therapy was evaluated by the usual clinical criteria, including duration of fever, improvement in neurological status, decrease in peripheral blood leukocyte count with a return of the differential count toward normal, and improvement in C.S.F. finding, including pressure, cell count, percentage polymorphonuclear leukocytes and glucose and protein content.

Subdural taps were performed whenever indicated (Platou, Rinker and Derick, 1959). In this report the outcome of therapy was evaluated according to the patient's course in the hospital and status at the time of discharge from the hospital. Untoward findings during the course of treatment in the hospital and any neurological abnormalities were recorded. "Delayed resolution clinically, but no sequelae at discharge" is a descriptive category which included patients with one or more findings such as: (a) transients subdural effusions, (b) convulsions persisting beyond the first 24 hours in the hospital, (c) persistence of a positive C.S.F. culture the day following admission to the hospital, (d) persistence or recurrence of C.S.F. pleocytosis, (e) documented persistence of nuchal rigidity or neurological findings such as cranial nerve palsies beyond five days even though resolution has occurred by the time of discharge. An additional "slow response" category incorporated the above plus other patients with no abnormality but fever persisting beyond five days of treatment.

(5) Bacteriological methods: Isolation and identification of the organisms were accomplished by conventional methods utilizing blood and chocolate agar, serum and thioglycollate broth and both aerobic and CO₂ incubation. Quellung was done in C.S.F. if adequate numbers of organisms were present. Bactericidal levels of ampicillin and chloramphenicol were determined using serial tube dilution techniques in GC medium containing 1% supplement B. (Difco).

RESULTS

Bacteriologic confirmation of the diagnosis of *H. influenzae* type B infection was complete in 68 of the 70 patients in the study group. Blood and C.S.F. cultures were both positive in 34 patients and organisms were cultured from the C.S.F. alone in the remaining 34. Two patients admitted with partially treated purulent meningitis had no positive cultures; they are included in this series on the basis of organisms seen of Gram's stain of the C.S.F. The cultural recovery of *H. influenzae* from 68/70 patients supported the assumption that antibiotic therapy given prior to admission had little effect on the course of the illness. To date, 164 strains of *H. influenzae* isolated from C.S.F. have been tested for *in vitro* sensitivity to ampicillin. Ninety-one per cent of the strains were killed by 0.4 µg./ml., and only two had bactericidal end points as high as 1.6 and 3.1 µg./ml. respectively.

The age and sex distribution of the patients studied is indicated in Table I. Two of the patients were more than 15 years of age. It should be noted that 14 of 26 patients in the ampicillin group were two years of age or older, and 13 of 44 patients in the control group were in this age group. This was believed to be an unimportant difference, since the distribution of severity of illness, according to the criteria in Table II, was similar within each age group and apparently