The neurological residua tabulated were those present at the time of discharge from the hospital, and may or may not have persisted. It is possible that in some instances additional defects will be found on careful follow-up study during subsequent years. It is important to note that there do not appear to be significant differences in proportion or severity of residual defects in any category between the study groups.

Evaluation of the side effects of therapy reveal no significant differences in the frequency of phlebitis, rash, eosinophilia >10%, or local reactions (Table 7). There was, however, a substantial difference (X^2=5.26; P=<0.05) in the frequency of signs of hematological toxicity. The most frequent change was a depression of reticulocytes, although granulocytopenia, and thrombocytopenia were also observed. Only 1 of 66 patients who received ampicillin for *H. influenzae* meningitis had a transient depression in granulocytes, whereas 17 of 107 who received chloramphenicol had hematological abnormalities. All of the hematological changes observed have been reversible, although in two patients in the chloramphenicol group granulocytic depression persisted for more than 2 months.

DISCUSSION

During the early period of the development of effective antimicrobial agents, it was apparent, without equivocation, that several caused substantial decreases in mortality and sequelae in bacterial meningitis. At the persent time, with numerous effective and relatively safe drugs available, selection of specific antibiotic agents for clinical use becomes more complex. These studies were conducted to determine whether it would be possible to simplify the therapy of acute bacterial meningitis, so that only a single compound could be used with results equivalent in safety and effectiveness to currently accepted therapy. Multiple drug therapy increases the hazards to the patient, as well as the expense of therapy, and, in addition, complicates nursing care. Since *H. influenzae* infection is often difficult to identify on direct examination of the spinal fluid, even by experienced personnel, it has been necessary frequently to administer either tetracycline (with attendant phlebitis with initial intravenous therapy or local reactions on subsequent intramuscular administration) or chloramphenicol (with a definite hematological hazard) to be certain that proper therapy is provided prior to confirmation by culture. It would appear that these studies demonstrating the efficacy of ampicillin offer an escape from this dilemma.

As one of the indices used in determining the response to an antibacterial regimen is the case fatality rate, it should be noted that this was 8.3% for the ampicillin group versus 11.8% in patients treated with conventional antibiotic routines. This difference was not significant, however, and may have been due entirely to the difference in age distribution of the pneumococcal group.

As noted above, all patients with detectable heart sounds on admission were included, whether or not aids to respiration were employed in transit, and whether or not cardiac arrest occurred within minutes. If one adjusts the overall mortality rate to exclude deaths occurring within the 12 hr immediately after admission, the corrected case fatality rate in the ampicillin group is 6.3% and among controls is 9.2%.

With regard to evidence of neurological residua, the rates were also similar in the two groups. Excluding fatalities, the proportions with residua at the time of hospital discharge was 13.6% among ampicillin-treated patients and 12.2% for the control group.

Ampicillin, although appearing to be somewhat more effective than chloramphenicol in vitro (Ivler et al., 1964), did not have a substantially greater clinical therapeutic benefit than chloramphenicol in *H. influenzae* meningitis. It is of interest, however, and consistent with the in vitro data, that six patients with *H. influenzae* meningitis had positive spinal fluid cultures 24 hr or more after initiation of chloramphenicol therapy, whereas none had similar positive cultures in the ampicillin category. The in vitro differences between benzylpenicillin and ampicillin against pneumococci and meningococci, were even less marked, but ampicillin appeared slightly more active (Ivler et al., 1964). It is interesting to note that three patients with pneumococcal meningitis and one with meningococcal meningitis had positive CSF cultures after 24 hr of therapy with benzylpenicillin, whereas none had positive cultures after 24 hr of ampicillin therapy.

While no significant differences were noted between the treatment groups with regard to phlebitis, skin rashes, local reaction, or eosinophilia, 17 patients (16%) who received chloramphenicol alone had evidence of hematological depression. Bone marrow examinations presented the classic picture of chloramphenicol tox-