of age or underlying illness such as alcoholism. Likewise, the persistence of organisms in patent P.H., who had a subdural effusion, might be explained by a drug diffusion problem. In the other five patients, there were no obvious explanations for persistence of viable organisms other than antibiotic interference. These five patients received a rapid intravenous infusion of penicillin and chloramphenicol on admission, followed by a continuous intravenous infusion containing the two antibiotics in our standard dosage (15). In contrast, no ampicillin-treated patients with the usual types of meningitis have had positive cultures after 24 hr of therapy. Similar observations, after 12 to 36 hr of therapy, have also been made by Fleming et al. (7) in a controlled study of the treatment of meningitis.

Lepper and Dowling (11), in comparing the two regimens which they employed, noted that the majority of deaths in the penicillin-treated group occurred within 48 hr of admission, whereas only 3 of the 11 patients who died while receiving combination therapy did so during the first 48 hr. An analysis of our patients revealed the same distribution (Table 3). Our observations would tend to substantiate the view that the effective single-drug and multiple-drug regimens both failed to effect recovery in a certain number of patients. In addition, multiple-drug herapy seems to have failed in potentially salvageable patients, presumably because of antibiotic interference.

It is somewhat surprising that in our study the only obvious difference between the single- and multiple-therapy groups was disability or death. One would have expected other differences, which might have been manifested in cerebrospinal fluid findings, days of fever, or hospital stay. Although no differences were apparent in the large groups, more detailed analyses of subgroups may be fruitful.

CONCLUSIONS

Many investigators have demonstrated the phenomenon of antibiotic antagonism in vitro and in experimental animals. Clinical examples of this phenomenon are restricted to a few situations in which the rapid bactercidal acton of an antibiotic is apparently necessary for a good response. Bacterial meningitis, particularly that which is severe on admission, appears to be one of the situations in which a combination of bacteriostatic and bactericidal agents is undesirable.

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