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APPENDIX X

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H. INFLUENZAE MENINGITIS: A CONTROLLED STUDY OF TREATMENT WITH AMPICILLIN

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THE case fatality rate in *Hemophilus influenzae* meningitis has been reduced to 5-10% by present methods of anti-bacterial and supportive therapy. As this rate is still far from optimal, the incidence of both early and late neurological sequelae is appreciable, and the antibiotics presently employed have definite and occasionally serious toxicity, new approaches to therapy must be evaluated.

Preliminary *in vitro* studies performed in our laboratory (Ivler, Thrupp, Leedom, Wehrle and Portnoy, 1963) indicated that 126 strains (118 type B) of *H. influenzae* isolated from cerebrospinal fluid (C.S.F.) were sensitive to ampicillin. Bacteriostatic and bactericidal levels did not differ significantly, and 91% were killed by 0.4 µg./ml. Only one had a bactericidal level as high as 1.6 µg./ml. In addition, sensitivities of meningococci and pneumococci to ampicillin were similar to those to penicillin G. These data, in conjunction with the apparent low toxicity of ampicillin suggested the trial of ampicillin as a single drug treatment for bacterial meningitis, in contrast to control groups treated with conventional therapy. The present report summarizes the experience to date with *H. influenzae* meningitis. Eighteen of these 70 patients were included in a preliminary report (Ivler *et al.*, 1963).

MATERIALS AND METHODS

(1) Selection of Patients: All patients more than two months of age with bacterial meningitis admitted to the Communicable Disease Service of the Los Angeles County General Hospital were included in the ampicillin study. Chart numbers assigned at the hospital central admitting office, and not subject to control of the ward physicians, were used to insure proper randomization. Patients with even (2, 4, 6, etc.) numbers were assigned to the ampicillin group while patients with chart numbers ending 1, 3, 5, etc., were given conventional therapy. During the period considered (June, 1963 to March 1964) a total of 72 patients were admitted with *H. influenzae* meningitis. Of these, 44 with odd chart numbers were assigned to the control group, and 28 with even numbers were eligible for ampicillin therapy. The difference in the size of the two groups was unexpected, although within the limits of chance variation. Two of the 28 patients were excluded from the ampicillin group, one by error in assignment and the other because of concomitant severe facial cellulitis following a dog bite where additional therapy was indicated. These two patients were not tabulated with either group. Most of the patients had received some antibacterial therapy prior to admission, usually subtherapeutic dosages, ineffective drugs, or both.

NOTE.—References at end of article.