

A total of 41 strains of *H. influenzae*, 12 of *D. pneumoniae*, and 15 of *N. meningitidis* were tested for their sensitivity to ampicillin. Varying numbers of these same strains were tested for their sensitivity to chloramphenicol, penicillin G, and tetracycline. All of the strains of *H. influenzae* were inhibited by ampicillin in a concentration of 0.78 mc. per milliliter or less, the majority by a concentration of 0.39 mcg. per milliliter. The MBC of ampicillin and penicillin G for pneumococci and meningococci were similar and ranged from 0.012 to 0.05 mcg. per milliliter for pneumococci and from 0.025 to 0.20 for meningococci.

Serum and spinal fluid ampicillin levels. Thirty eight simultaneous serum and spinal fluid samples were obtained one hour after a parenteral dose (intravenously or intramuscularly) of ampicillin. Eight of the paired specimens were from patients with no evidence of meningeal disease, 10 from patients with viral meningitis or encephalitis, and 20 from patients with bacterial meningitis. Ampicillin levels in the serum and spinal fluid were assayed by Bristol Laboratories using the cup-plate method with *Sarcina lutea* as the test organism. The relationship between the dose of ampicillin and the cerebrospinal fluid and serum levels could not be assessed in this series of patients because of variations in dosage and route of administration. However, data are presented to demonstrate the ratios between simultaneous cerebrospinal fluid and serum levels (Tables II and III). The dose employed varied from 25 mg. per kilogram (150 mg. per kilogram per day divided into 6 doses) to 50 mg. per kilogram (250 mg. per kilogram per day divided into 6 doses). The paired samples were obtained one hour after administration of the dose and all patients had been on the drug for a period of 1 to 4 days at the time of sampling.

Satisfactory serum levels were obtained in all instances and ampicillin was detectable in each spinal fluid specimen. However, there was a striking differential between the simultaneous cerebrospinal fluid and serum levels. The highest mean cerebrospinal fluid-to-serum ratio (expressed as percentage) was obtained in patients with bacterial meningitis (11 per cent) while the ratio in the patients with viral meningitis was 9 per cent and in patients without evidence of meningitis was 4 per cent. Although the mean cerebrospinal fluid ampicillin levels in the patients with bacterial meningitis and the group without evidence of meningitis, 1.9 mg. per milliliter and 0.8 mg. per milliliter, are not significantly different ($p > 0.1$), the mean ratios in those two groups of patients, 11 and 4 per cent, respectively, are significantly different ($p < 0.01$.)

TABLE II.—SIMULTANEOUS BLOOD AND CEREBROSPINAL FLUID AMPICILLIN LEVELS IN 8 PATIENTS WITH NORMAL MENINGES AND IN 10 PATIENTS WITH VIRAL MENINGOENCEPHALITIS

Route and frequency of administration	CSF level (mg./ ml.)	Blood level (mg./ ml.)	Ratio (CSF/ blood)	Total daily dose (mg./ kg./day)	Individual dose (mg./ kg.)	Time of CSF and blood sam- pling after drug given (hour)
Normal meninges:						
Intramuscularly every 6 hours.....	0.1	20.0	0.005	150	38	1
Do.....	.3	29.0	.010	150	38	1
Do.....	.3	25.0	.012	150	38	1
Do.....	.3	14.0	.021	225	56	1
Intramuscularly every 4 hours.....	.8	57.0	.014	150	25	1
Intramuscularly every 6 hours.....	.8	25.0	.032	170	43	1
Intravenously every 4 hours.....	.9	14.0	.064	150	25	1
Do.....	2.9	15.0	.193	150	25	1
Mean.....	.8	24.9	.044			
Percent.....			(4.4)			
Viral meningitis:						
Intramuscularly every 6 hours.....	.2	36.0	.006	150	38	1
Intramuscularly every 4 hours.....	.4	4.4	.091	150	25	1
Do.....	.5	14.0	.036	150	25	1
Do.....	.5	14.0	.036	150	25	1
Do.....	.5	12.0	.042	150	25	1
Intramuscularly every 6 hours.....	.6	29.0	.021	150	38	1
Do.....	.6	22.0	.027	150	38	1
Intramuscularly every 4 hours.....	1.2	20.0	.060	150	25	1
Intramuscularly every 4 hours.....	3.7	15.0	.247	150	25	1
Intravenously every 4 hours.....	3.8	11.0	.345	150	25	1
Do.....						
Mean.....	1.2	17.7	.091			
Percent.....			(9.1)			