

REFERENCES

1. Berman, P. H., and Banker, B. Q. Neonatal meningitis. *Pediatrics*, 38: 6-24, 1966.
2. Eichenwald, H. F. Some observations on dosage and toxicity of kanamycin in premature and full term infants. *Ann. N. Y. Acad. Sci.* 132: 984-991, 1965.
3. Ivler, D., Thrupp, L. D., Leedom, J. M., Wehrle, P. F., and Portnoy, B. Ampicillin in the treatment of acute bacterial meningitis. *Antimicrob. Agents Chemother.* 3: 335-345, 1964.
4. Leedom, J. M., Ivler, D., Mathies, A. W., Thrupp, L. D., Portnoy, B., and Wehrle, P. F. Importance of sulfadiazine resistance in meningococcal disease in civilians. *New Eng. J. Med.*, 273: 1395-1401, 1965.
5. Lepper, M. H., and Dowling, H. F. Treatment of pneumococcal meningitis with penicillin compared with penicillin and Aureomycin. *Arch. Intern. Med.* (Chicago), 88: 489-494, 1951.
6. Lepper, M. H., Dowling, H. F., Wehrle, P. F., Blatt, N. H., Spies, H. W., and Brown, M. Meningococcal meningitis, treatment with large doses of penicillin compared to treatment with Gantrisin. *J. Lab. Clin. Med.*, 40: 891-900, 1952.
7. Lithander, A. The passage of penicillins into the cerebrospinal fluid and brain in experimental meningitis: experimental investigations on rabbits. *Postgrad. Med. J.*, suppl. 40 112-119, 1964.
8. Mathies, A. W., Jr., Crockett, V., Teberg, A., and Friedman, D. B. Unpublished data.
9. Mathies, A. W., Leedom, J. M., Thrupp, L. D., Ivler, D., Portnoy, B., and Wehrle, P. F. Experience with ampicillin in bacterial meningitis. *Antimicrob. Agents Chemother.*, 5: 610-617, 1966.
10. Nyhan, W. L., and Richardson, F. Complications in meningitis. *Ann. Rev. Med.*, 14: 243-260, 1963.
11. Proceedings of the Research Conference on the Prevention of Mental Retardation, University of Texas, 1966, edited by H. F. Eichenwald. United States Public Health Service, Washington, D.C., in press.
12. Thrupp, L. D., Leedom, J. M., Ivler, D., Wehrle, P. F., Brown, J. F., Mathies, A. W., and Portnoy, B. H. *Influenzae* meningitis: a controlled study of treatment with ampicillin. *Postgrad. Med. J.*, suppl. 40 119-126, 1964.
13. Thrupp, L. D., Leedom, J. M., Ivler, D., Wehrle, P. F., Portnoy, B., and Mathies, A. W. Ampicillin levels in the cerebrospinal fluid during treatment of bacterial meningitis. *Antimicrob. Agents Chemother.*, 5: 206-213, 1966.

QUESTIONS AND ANSWERS

QUESTION: What do you consider adequate treatment when: (1) an organism is not found on the initial spinal fluid examination, and (2) the patient is not responding to treatment started elsewhere, also without having isolated the organism?

DR. WEHRLE: This is a situation that we face in about one-third of the patients who come to us for treatment. In 50 to 60 per cent of the patients we can identify the organism at the time of admission to the hospital with a direct Gram stain. This figure may be increased slightly when one adds to the Gram stain the results of the fluorescent antibody technique. This leaves a substantial portion who must be treated without a definite diagnosis since only about 10 per cent of patients with no organisms identified on smear will have a positive culture.

We have studied a standard approach in two different age groups. For those cases from birth through 2 months of age, we start with either penicillin or ampicillin in doses equivalent to about 75 mg. per kg. per day of ampicillin after an initial loading dose of one-third of that and kanamycin at a dose of 15 mg. per kg. per day. In these very young infants there are a great many different organisms that may be causing the infection, and in our experience about 95 to 97 per cent of all of these organisms are inhibited by this particular combination.

In patients 2 months of age and older who do not have a dermal sinus, endocarditis, previous neurosurgical procedures, ventriculovenous shunt, or other factors that might be associated with an unusual organism, ampicillin alone appears to be more effective than the combination of chloramphenicol and penicillin with or without the addition of streptomycin.

It should be noted that the mortality rate in whom you do not see the organism on smear is lower than in those where the organism is identified. The only exception to this is the Waterhouse-Friderichsen syndrome in meningococcal infection. Also, the very young or very old individual with a fulminant