

pneumococcal meningitis may have little or no appreciable cellular response. Organisms may be seen in the spinal fluid, although if an antibiotic has been given this may prevent cultural identification of the organism.

QUESTION: What criteria do you use for discontinuing antibiotic therapy?

Dr. WEHRLE: Our procedure is to treat intensively with full dosage of antibiotics for the required period. We do not reduce dosage during the course of therapy. We continue full dosage until the patient has been afebrile for about 5 days, which is usually about 2 weeks after treatment is started. At that point a repeat spinal puncture is done and if the cell count is less than 30 white blood cells per cm., and, if the protein is less than 50 mg. per cent, we discontinue antimicrobial therapy, watch the patient for 2 days in the hospital, and then send him home. We do not believe that low dosage of antibiotics over an additional 1- to 2-week period or longer does anything other than to mask those infections that have not been treated adequately. With young infants we do not discontinue therapy until at least 3 weeks have gone by. If the protein or cell count remains up, even though there are no neurological changes, treatment should be continued.

Relapses occur in two or three kinds of situations. One is with a Gram-negative infection either in young infants or in individuals whose immune defenses are impaired regardless of age. In several hundred meningococcal infections we have yet to see a relapse. A relapse after pneumococcal meningitis is extremely rare, and if relapse occurs it is usually associated with mastoiditis or abscess. Occasionally *Hemophilus influenzae* infections will recur, particularly in the very young infant.

QUESTION: How do you explain the lower mortality rate with ampicillin alone compared with combination antibiotic therapy?

Dr. WEHRLE: There are three possibilities that might explain this. It could be a chance variation. This study was an alternate control using odd and even chart numbers. The (χ^2) is 6 with a p value of nearly 0.01 so that maybe this is the one change in 100. The second possibility is that the toxicity of chloramphenicol when used in an already sick patient caused an adverse effect. Certainly this drug has been amply shown to cause serious difficulties in young infants, and it was responsible, at least in part, for the increased mortality rate in infants during the wave of the staphylococcal problem when large doses of chloramphenicol were being used. The third possibility is that there may be some kind of interference between the drugs. However, antimicrobial interference between a primarily bacteriostatic drug such as chloramphenicol or tetracycline and a primary bactericidal drug such as penicillin has certainly not been important in clinical medicine. We are still puzzled by this finding and will continue to investigate it.

QUESTION: What drugs are now given intrathecally?

Dr. WEHRLE: We consider three drugs as the only ones that we will use by this route: kanamycin, on occasion; polymyxin, invariably if you must use polymyxin for therapy in *Pseudomonas* infection or on the basis of the particular sensitivity of an unusual organism; and amphotericin. I would like to emphasize that there is no purpose in giving intrathecal medication, if the spinal fluid culture and Gram stain are negative 24 to 36 hours after you put the patient on therapy, because you are achieving an adequate suppressant effect with the particular systemic antimicrobial agent used.

QUESTION: What is the place of prophylactic antibiotics in basal skull fracture?

Dr. WEHRLE: I would like to state here one concern that I have with regard to prophylaxis. One can cause a shift in the nasopharyngeal flora to Gram-negative organisms including *Escherichia coli*, *Pseudomonas*, *Klebsiella-Aerobacter*, or a number of other organisms in the nasopharynx of individuals who are receiving penicillin or other prophylactic antibiotics at a level at which they would be expected to eradicate the pneumococcus and really be effective prophylactic therapy. I see no value in this type of therapy.

QUESTION: What central nervous system dysfunction has been seen with ECHO viruses?

Dr. WEHRLE: We have confirmation in some patients that ECHO viruses have been associated with definite muscle weakness with a relatively mild poliomyelitis-type pattern of anterior horn cell disease. We have tried to reproduce this disease in monkeys, not successfully as yet, but we plan to go further with this. Only certain strains of ECHO viruses 4, 6, and 9 have been clearly implicated. Acute cerebellar ataxia has also been associated with ECHO-9 infection.