The Treatment of Bacterial Meningitis

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Despite recent advances in treatment, mortality and morbidity associated with bacterial meningitis remains high. A satisfactory approach to this condition will be realized only with prevention. Research into chemoprophylaxis, but more importantly active immunization, is taking place and is discussed elsewhere in this issue. This review will deal only with the antibiotic treatment of bacterial meningitis.

NEONATAL BACTERIAL MENINGITIS

Group B Streptococcus, gram-negative bacilli, especially Escherichia coli and Listeria monocytogenes are the major pathogens encountered in this age group. Consequently, combination therapy using a penicillin such as ampicillin and an aminoglycoside is usually initiated pending culture results. Antibiotics are generally continued for 2 weeks beyond the time that sterility of the cerebrospinal fluid is achieved. When group B Streptococcus is recovered, penicillin therapy is continued. Although accelerated killing of group B Streptococcus was demonstrated in vitro when gentamicin was added to ampicillin, the role of adding or continuing an aminoglycoside for treatment is unclear.2

Gram-negative bacillary meningitis is largely, although not exclusively, a disease of neonates, and carries a particularly poor prognosis. Consequently, several approaches have been tried, but unfortunately none have been found to be clearly superior to the use of ampicillin and an aminoglycoside. Neither intrathecal nor intraventricular aminoglycoside administration were found to be of any benefit in treating this condition.3,4 Theoretically, the third-generation cephalosporins should be particularly useful because of their excellent activity against these pathogens as well as their penetration into the cerebrospinal fluid (CSF).5 No difference was observed in outcome, though, when 63 infants with gram-negative bacillary meningitis were treated with ampicillin and amikacin as opposed to ampicillin and moxalactam.6

INFANTS AND CHILDREN

The major pathogens encountered beyond the neonatal period include Haemophilus influenzae type b (Hib), Streptococcus pneumoniae, and Neisseria meningitidis. Since 1964, ampicillin has been the mainstay of therapy. In 1974, beta-lactamase producing Hib were...
reported and chloramphenicol was added to ampicillin for the initial therapy of bacterial meningitis. During the last 2 years several new cephalosporins have been introduced which again enable the physician to utilize a single drug in treating meningitis in this age group.

**DURATION OF THERAPY**

The standard length of therapy for bacterial meningitis beyond the neonatal period has been 10 days, except for *Neisseria meningitidis* where 7 days is satisfactory. The entire course of therapy is administered by the parenteral route except for chloramphenicol, where oral therapy is actually preferred. Recently two groups of investigators have found that 7 days of therapy may also be satisfactory for uncomplicated *Hib* meningitis.\(^7\)\(^8\) In the Dallas study the authors cautioned against the shorter course of therapy for group B streptococcal or coliform meningitis, patients with persistent signs of meningeal inflammation, or in those patients with markedly abnormal CSF exams at the completion of therapy. Previous studies that have evaluated repeat CSF examinations at the completion of therapy have not found such exams to be helpful in deciding on length of therapy or outcome.\(^9\)\(^10\)

**SELECTION OF AN AGENT**

When deciding on an agent to be used in treating meningitis, the physician might consider several factors. Treatment with the traditional agents, ampicillin and chloramphenicol, has been associated with a lack of drug failure and a minimal number of side effects since 1964. Although physicians are, in general, very familiar with the use of these drugs, several points need to be emphasized in this regard. As discussed elsewhere in this issue, chloramphenicol must be used with care. When given intravenously, chloramphenicol succinate must be hydrolyzed before it is converted to the active compound, chloramphenicol. This occurs at a variable and at times unpredictable rate, and consequently oral therapy is preferred and serum levels must be monitored when chloramphenicol is relied on for therapy. In addition, when used with drugs such as phenobarbital, diphenhydantoin or rifampin, the pharmacokinetics of chloramphenicol are further altered as indicated elsewhere in this issue.

Several of the newer cephalosporins enable the physician to use a single drug as the treatment for meningitis. Cefuroxime and cefotaxime are active against all three of the pathogens responsible for meningitis beyond the neonatal period. When used to treat meningitis, both of these agents have been found to be as effective as traditional therapy and largely free of side effects.\(^11\)\(^12\) Ceftriaxone differs from the other two drugs in having a significantly longer half-life. It too has been found to be as effective as traditional therapy, and currently when used for meningitis, it is administered twice daily.\(^13\)\(^14\) Ceftriaxone has also been used in a single daily dose for meningitis.\(^15\) This might eventually prove useful in those situations where the maintenance of intravenous access is difficult or toward the end of therapy when completion of the course of therapy as an outpatient is contemplated.

**PATTERNS OF RESISTANCE**

The susceptibility of the commonly encountered pathogens has changed significantly in the last 15 years. It is commonly appreciated that 20% to 30% of *Hib* are beta-lactamase producers and consequently resistant to ampicillin. In addition, occasional strains of *Hib* are now being encountered that also produce acetyl transferase rendering the organism resistant to chloramphenicol. Some strains are both beta-lactamase and acetyl transferase producers. These strains account for approximately 18% of *Hib* encountered in Spain and approximately 60 such isolates have been seen in the United States.

*Streptococcus pneumoniae* are no longer uniformly susceptible to penicillin or ampicillin with 3% to 16% of *S. pneumoniae* exhibiting "relative resistance" with minimal inhibitory concentrations (MICs) of penicillin of 0.1-1 μg/ml. When these strains cause disease in the central nervous system, alternatives to penicillin or ampicillin must be used. The laboratory can reliably establish that a particular *S. pneumoniae* is relatively resistant when the sensitivity is determined utilizing an oxacillin disc. Conventional penicillin discs containing 10 units of penicillin do not reliably distinguish between susceptible and relatively resistant strains. When an oxacillin disc is utilized, strains continued on page 460
BACTERIAL MENINGITIS

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...exhibiting relative resistance to penicillin will usually manifest no zone of inhibition of growth and are thus easily distinguished from susceptible strains. Neisseria meningitidis has remained uniformly sensitive to penicillin with a single exception.16

In summary, several antibiotic regimens are available to the physician treating the patient with bacterial meningitis. On occasion one of these regimens may be preferred, depending on the susceptibility of the infecting organism, concomitant drugs being administered, the availability of laboratory support for monitoring drug levels, or the ability to maintain intravenous access.

REFERENCES