

# Bacterial Meningitis in Older Neonates

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• During a five-year period, 24 patients' conditions (age range, 2 to 6 weeks) were diagnosed, and they were treated for bacterial meningitis. Organisms recovered from the CSF included group B *Streptococcus* (n=6), *Escherichia coli* (n=5), *Listeria monocytogenes* (n=5), *Hemophilus influenzae* (n=4), *Streptococcus pneumoniae* (n=2), and group D and group A *Streptococcus* (one each). Initial antimicrobial therapy must include antibiotics that are effective across this spectrum of potential pathogens. Symptoms and signs were often subtle. Six children (25%) experienced major neurologic residua, including five patients (21%) in whom hydrocephalus developed. Ultrasound examination of the head at the end of therapy was an effective technique for early assessment of neurologic sequelae.

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The cause and treatment of bacterial meningitis in neonates from birth to 28 days have been well established.<sup>1,2</sup> Similarly, there have been considerable data in older infants and children.<sup>3</sup> In newborns, group B *Streptococcus*, gram-negative coliforms, and *Listeria monocytogenes* are the most common pathogens, and in older infants and children, *Hemophilus influenzae*, *Streptococcus pneumoniae*,

and *Neisseria meningitidis* are most frequent as causes of meningitis. To our knowledge, no study has focused on the cause of meningitis in patients aged 2 to 6 weeks. Selection of antibiotics has varied from those agents primarily effective against the pathogens encountered in newborns to the more common regimens designed for the bacteria encountered in the older pediatric patients.

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See also pp 1043 and 1055.

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We reviewed our experience with meningitis in older neonates (2 to 6 weeks of age) during a five-year period (1977 to 1982) to determine the cause of meningitis in this age group and to delineate signs, symptoms, and factors affecting the prognosis that might be unique to these patients.

## PATIENTS AND METHODS

Between 1977 and 1982, 24 patients between 2 and 6 weeks of age with bacterial meningitis were treated at the Arkansas Children's Hospital, Little Rock. The diagnosis of bacterial meningitis was confirmed by positive culture of CSF or by detection of antigen (counterimmunoelectrophoresis or coagglutination). Fourteen patients with bacterial infection, following placement of ventriculoperitoneal shunts, and 11 prematurely born patients with complicated neonatal courses were excluded.

Diagnostic evaluation included cultures of CSF, blood, and urine and bacterial antigen detection in CSF, serum, and urine.<sup>4</sup> Lumbar punctures were repeated at 24 or

48 hours and, in most cases, 24 hours after termination of antimicrobial therapy. Additional routine initial laboratory data included a complete blood cell count, serum electrolyte determinations, serum urea nitrogen level, blood glucose level, and urinalysis. Inappropriate antidiuretic hormone (ADH) secretion was monitored with daily weights, frequent examination of urine for specific gravity, osmolality, and sodium, along with daily serum electrolyte and osmolality determinations until patients were stable, usually after three to four days of treatment. Those patients with demonstrated inappropriate ADH secretion were restricted to 75% of maintenance fluids. Twice daily, patient assessment focused on clinical changes, such as fever, meningism, sensorium, irritability, and neurologic function.

Antimicrobial therapy for these patients was variable and included the following: ampicillin sodium and gentamicin sulfate, ampicillin and chloramphenicol sodium succinate, or ceftriaxone sodium alone. Information on many of these patients has been previously reported.<sup>5,6</sup> Hearing and visual deficits were assessed by EEG-monitored responses to appropriate stimuli. Social service evaluation was conducted for all children, and necessary services were provided. All patients were examined by both infectious disease and neurology consultants during short-term hospitalization and at follow-up.

Longitudinal follow-up after hospitalization for two to four weeks consisted of the multidisciplinary approach given in Table 1.

All patients were followed up personally by one of us (R.W.S.) intermittently for six months to five years. Additional information was provided by private pediatricians for progress and status after the acute infection. Ultrasound examination of the

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**Table 1.—Protocol for Longitudinal Treatment of Bacterial Meningitis**

Before discharge
Audiologic examination (auditory evoked responses)
Visual assessment (visual evoked responses)
Developmental screening
Social services consultation
Ultrasound examination
2 wk
Physical examination, neurologic evaluation
2 mo
Physical examination, neurologic evaluation
Audiologic examination
Developmental screening
Social services consultation
Complete blood cell count (for anemia or those patients receiving chloramphenicol sodium succinate)
6 mo and 1 yr
Physical examination, neurologic evaluation

CNS was performed in standard fashion by the Department of Radiology, Arkansas Children's Hospital.

**RESULTS**

The bacteria recovered from 24 patients are given in Table 2. A wide spectrum of organisms was isolated. Some differences in origin were observed for infants at specific ages. In this limited series, all five infants with *Listeria* meningitis were 2 to 3 weeks of age. Both patients with pneumococcal meningitis were 5 weeks old. *Escherichia coli* or *H influenzae* occurred as frequently in the 2- to 4-week-old infants as in those 4 to 6 weeks of age.

The 24 infants' initial signs and symptoms were as follows:

Sign/Symptom	No. (%) of Patients
Fever	19 (79)
Irritability	19 (79)
Anorexia/vomiting	12 (50)
Diarrhea	7 (29)
Lethargy	6 (25)
Nuchal rigidity	4 (17)
Respiratory distress	4 (17)
Abdominal distention	4 (17)
Seizure	4 (17)
Bulging fontanelle	3 (13)
Apnea	3 (13)
Jaundice	2 (8)

As shown in the previous tabulation, nuchal rigidity and a bulging fontanelle were usually not evident, occur-

**Table 2.—Organisms Recovered From CSF in 24 Patients, Aged 2 to 6 Weeks, With Bacterial Meningitis**

Organism	No. of Patients	Age, wk
Group B <i>Streptococcus</i>	6	2, 2, 3, 3, 5, 5
<i>Escherichia coli</i>	5	2, 3, 4, 5, 5
<i>Listeria</i>	5	2, 2, 2, 2, 2
<i>Hemophilus influenzae</i>	4	2, 3, 4, 4
<i>Streptococcus pneumoniae</i>	2	5, 5
Group D <i>Streptococcus</i>	1	2
Group A <i>Streptococcus</i>	1	2

**Table 3.—Mortality and Morbidity in 24 Patients, Aged 2 to 6 Weeks, With Bacterial Meningitis**

	No. (%) of Patients	Organism
Death	1 (4)	Group B <i>Streptococcus</i>
Morbidity	6 (25)	...
Hydrocephalus	5 (21)	2 <i>Hemophilus influenzae</i> , 2 <i>Listeria monocytogenes</i> , 1 group B <i>Streptococcus</i>
Hearing deficit	2 (8)	<i>H influenzae</i> , group B <i>Streptococcus</i>
Seizure disorder	2 (8)	<i>H influenzae</i> , group B <i>Streptococcus</i>
Focal neurologic disorder	2 (8)	<i>H influenzae</i> , group B <i>Streptococcus</i>

ring in only 17% and 13% of our patients, respectively. Fever and irritability were most consistently noted; both were present in 79%. Seizures and apneic episodes were each observed in one patient during hospitalization. Nonspecific gastrointestinal symptoms, such as anorexia, vomiting, diarrhea, and abdominal distention, were frequent.

A 5-week-old infant with group B streptococcal disease died who had a cardiopulmonary arrest shortly after admission. Six other infants (25%) had significant residua (Table 3). Hydrocephalus developed in five infants and was diagnosed within four weeks of the onset of disease. Two instances of hydrocephalus were discovered by ultrasound examination of the CNS; one infant had no increase in head circumference before the ultrasound study.

The mean duration of symptoms before admission was 1.8 days, with a range of eight hours to six days. The symptoms in the present patients were often more subtle than the classic triad of fever, meningism, and bulging fontanelle, characteristic of older patients. Nineteen patients (79%) manifested inappropriate ADH secretion during hospitalization.

Our patients have had longitudinal follow-up ranging from six months to five years. All significant residua were apparent by two months after treatment (Table 1).

**COMMENT**

This clinical series demonstrates that there is a wide spectrum of bacterial agents that causes meningitis in patients aged 2 to 6 weeks. When only neonates (birth to 28 days of age) are considered, group B *Streptococcus*, *E coli*, and *L monocytogenes* are the three most commonly recovered pathogens.<sup>7</sup> However, the relative frequency of *H influenzae* (17%) and *S pneumoniae* (8%) was much higher in our 2- to 6-week-old age group than that reported in neonates. In contrast with disease in infants, *H influenzae* was less common, and *N meningitidis* was not seen. *Escherichia coli* meningitis was frequent in the older neonate—a fact that previous reviews of neonatal meningitis have not noted. A higher incidence of *E coli* meningitis during the first two weeks of life has been reported.<sup>2,7</sup>

The high frequency of severe morbidity in this age group is disturbing and may not have been recognized pre-

viously. Long-term follow-up indicates that all patients with hydrocephalus, seizure disorders, and focal neurologic disorders now exhibit significant mental or physical handicaps; these infants make up 25% (six) of our present series. Early detection and intervention with provision of hearing aids for the two patients with residual-hearing defects has helped to prevent speech and learning disabilities.

The low mortality (4%) probably reflects progress in intensive care management and adequate antibiotic treatment. Increased survival rates may result in survivors experiencing subsequent severe neurologic disability.

Duration of symptoms before admission was similar to older cases of meningitis at our institution. Although symptoms in these younger patients were often more subtle, there did not seem to be an inordinate delay in the diagnosis of meningitis.

In younger infants and neonates with open fontanelles, ultrasound examination of the CNS is less expensive and equally sensitive as compared with computed tomography for demonstrating hydrocephalus.<sup>8,9</sup> We have incorporated ultrasound as a routine examination shortly before hospital discharge, as this test may disclose hydrocephalus before this is evident by serial head circumference measurements.

Longitudinal treatment of infants with meningitis is essential for adequate care, particularly in light of the high incidence of severe morbidity detailed in our study. Our approach is

given in Table 1. All residua were detected in patients at 2 months of age. Clinic visits after this time were most productive in providing continuing guidance for medical treatment of previously defined neurologic sequelae. Patients can be treated as normal if, at 2 months of age, neurologic, audiologic, and visual measurements are normal. Anemia, common after severe infection, can also be treated during longitudinal follow-up. Involvement of social services is essential not only for the medically indigent, but also to make others aware of resources available to everyone for continued medical care once a neurologic deficit is recognized.

The initial selection of appropriate antibiotics for meningitis in the 2- to 6-week-old age group is difficult because of the diversity of bacteria encountered (Table 2). Ampicillin and an aminoglycoside would be inadequate for some strains of *H influenzae*. Ampicillin and chloramphenicol would not be optimal for ampicillin-resistant *E coli*; two of the five *E coli* isolates in the present series were resistant to ampicillin. Poor penetration of aminoglycosides into the CSF prevent optimal treatment of sensitive pathogens, such as *E coli*.

The newer  $\beta$ -lactam antibiotics, moxalactam disodium or cefotaxime sodium, in combination with ampicillin may be effective for almost all pathogens encountered in this age group. However, neither moxalactam nor cefotaxime is effective against *Listeria* or group D *Streptococcus* (enterococcus). Ampicillin is the preferred agent

for treating infections caused by these organisms. Moxalactam is inadequate for group B *Streptococcus* and *S pneumoniae* (pneumococcus); ampicillin is effective.

In summary, we currently recommend a combination of ampicillin plus either cefotaxime or moxalactam for the treatment of meningitis in 2- to 6-week-old pediatric patients.

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## References

1. McCracken GH Jr, Shinefield HR: Changes in the pattern of neonatal septicemia and meningitis. *Am J Dis Child* 1966;112:33-39.
2. Feigin RD: Central nervous system infections, in Feigin RD, Cherry JD (eds): *Textbook of Pediatric Infectious Disease*. Philadelphia, WB Saunders Co, 1981, pp 293-308.
3. Maguire GF, Myers MG: Antimicrobial selection for meningitis in young infants. *Am J Dis Child* 1979;133:1132-1137.
4. Kaplan SL, Feigin RD: Rapid identification of the invading microorganism: Symposium on the laboratory in pediatric practice. *Pediatr Clin North Am* 1980;27:783-803.
5. Steele RW, Eyre LB, Bradsher RW, et al: Pharmacokinetics of ceftriaxone in pediatric patients with meningitis. *Antimicrob Agents Chemother* 1983;23:191-194.
6. Steele RW, Bradsher RW: A comparison of ceftriaxone to standard therapy for bacterial meningitis. *J Pediatr*, in press.
7. Robbins JB, McCracken GH Jr, Gotschlich EC, et al: *Escherichia coli* K1 capsular polysaccharide associated with neonatal meningitis. *N Engl J Med* 1974;290:1216-1220.
8. Horbar JD, Leahy K, Lucey JF: Real-time ultrasonography: Its use in diagnosis and management of neonatal hydrocephalus. *Am J Dis Child* 1982;136:693-696.
9. Hill A, Shackelford GD, Volpe JJ: Ventriculitis with neonatal bacterial meningitis: Identification by real-time ultrasound. *J Pediatr* 1981; 99:133-136.