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## 50 Years Ago in *THE JOURNAL OF PEDIATRICS*

### Revisiting a Diagnostic Dilemma 50 Years Later: Partially Treated Bacterial Meningitis

Winkelstein JA. The Influence of Partial Treatment with Penicillin in the Diagnosis of Bacterial Meningitis. *J Pediatr* 1970;77:619-24.

Cerebrospinal fluid (CSF) analysis and culture remain the gold standard diagnostic evaluation for bacterial meningitis. However, early initiation of antibiotics may complicate the interpretation of subsequently obtained CSF, rendering it difficult to distinguish viral from bacterial meningitis. A landmark study in 1970 challenged this presumption. Winkelstein tested whether procaine penicillin, the drug most commonly prescribed for febrile children in a community in Alaska, would modify CSF findings and obfuscate the diagnosis. The records of 21 children who had received penicillin were compared with 16 who had not received penicillin before their diagnostic lumbar puncture. There was no significant effect of antibiotic pretreatment on clinical presentation, CSF variables, or ability to differentiate bacterial from viral meningitis. However, the predominant bacterial etiology in that study was *Haemophilus influenzae*.

Today, however, the epidemiology of pediatric bacterial meningitis has changed, reflecting the success of vaccines for *H influenzae*, *Streptococcus pneumoniae*, and *Neisseria meningitidis*. Although *H influenzae* has been eradicated, pneumococcal and meningococcal disease persist owing to incomplete vaccine protection against all serotypes. This in turn, has led to the emergence of nonvaccine serotypes as causative pathogens. Furthermore, there are no vaccines for group B streptococcus, staphylococcus, or *Escherichia coli*, which have increasingly become more important causes of meningitis, particularly in infants.

Additionally, newer antimicrobials such as third-generation cephalosporins and carbapenems have supplanted penicillins, which has important implications for CSF interpretation. For example, ceftriaxone achieves higher central nervous system concentrations and has been shown to rapidly sterilize CSF, even after 1 dose for *N meningitidis*. These newer antibiotics may also cause a more rapid shift from a neutrophilic-to a monocytic-predominant CSF profile, although there is persistence of pleocytosis and elevated protein levels.

The clinical imperative or temptation to initiate antibiotics has become more “common practice,” particularly in settings where a lumbar puncture is difficult to perform or unsuccessful. The lack of microbiological CSF data poses a diagnostic challenge hindering opportunities for appropriate antibiotic stewardship. This issue has been especially evident in managing infants treated for *E coli* urosepsis where interpretation of pretreated CSF is limited. Newer molecular diagnostic tools including broad-range polymerase chain reaction targeting the 16S ribosomal RNA gene of bacteria are promising, but more research is required. Despite great advances, the challenge of partially treated bacterial meningitis endures.

**Brenda I. Anosike, MD, MPH**

Boston Children's Hospital  
Boston, Massachusetts

**Betsy C. Herold, MD**

Children's Hospital at Montefiore  
Albert Einstein College of Medicine  
Bronx, New York