

the receiver operating characteristic curve for white blood cell count unadjusted and adjusted by all methods were similar. Adjusting CSF white blood cell counts to account for increased red blood cells did not improve diagnostic utility and resulted in decreased sensitivity with marginal gain in specificity.

Conclusions Adjustment of white blood cell counts in the setting of a traumatic lumbar puncture does not aid in the diagnosis of culture- or Gram stain-proven bacterial and fungal meningitis in neonates.

Commentary As acknowledged by the authors, incomplete data for recent exposure to antibiotics (transplacental or neonatal) precluded their ability to assess the potential importance of that factor. Use of positive culture or Gram stain of CSF as the “gold standard” for bacterial or fungal meningitis limited confounding by false-negative culture results because of prior antibiotic therapy, but the high frequency of pretreatment in many nurseries would make analysis of CSF from such subjects particularly useful. The lack of complete data regarding intracranial hemorrhage similarly precluded evaluation of the contribution of consequent arachnoiditis to elevated CSF white blood cell counts in the absence of positive culture or Gram stain. The conundrum posed by coagulase-negative staphylococci as potential contaminant versus true pathogen is recognized and considered separately. Clinicians should recall that CSF with white blood cell counts below the diagnostic threshold does not preclude central nervous system infection. CSF obtained very early after meningeal invasion may reflect insufficient time for generation of an inflammatory cellular response or development of adequate pathogen burden for positive Gram stain. Additionally, slow transport of CSF to the laboratory for analysis may be accompanied by loss of leukocyte viability and a drop in the apparent number of white blood cells.¹ Brain abscess and other parenchymal or vascular infectious foci that are not adjacent to CSF-containing spaces may also produce no evident CSF abnormalities. When to perform lumbar puncture in sepsis evaluation remains controversial, although the high frequency of positive CSF culture with negative blood culture in very low birth weight infants >3 days old suggests liberal use of lumbar puncture in such infants.² These authors present a convincing argument that when CSF is obtained, correction of white blood cell count for excess red blood cells ($\geq 500/\text{mm}^3$) is unnecessary and potentially misleading. An elevated CSF white blood cell count should prompt serious consideration of selection, dosage, and duration of antibiotic therapy appropriate for meningitis even when culture is unrewarding.

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References

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Pneumococcal vaccine reduces the rates of pneumococcal meningitis in children

Hsu HE, Shutt KA, Moore MR, Beall BW, Bennett NM, Craig AS, et al. Effect of pneumococcal conjugate vaccine on pneumococcal meningitis. *N Engl J Med* 2009;360:244-56.

Question What has been the effect of the pediatric heptavalent pneumococcal conjugate vaccine (PCV7) on pneumococcal meningitis since its introduction in 2000?

Design Population-based surveillance study.

Setting Eight active bacterial core surveillance sites in the United States

Participants Patients with pneumococcal meningitis, diagnosed between 1998 and 2005.

Outcomes Changes in the incidence of pneumococcal meningitis from 1998 through 2005 were assessed against baseline values from 1998–1999. Isolates were grouped into PCV7 serotypes (4, 6B, 9V, 14, 18C, 19F, and 23F), PCV7-related serotypes (6A, 9A, 9L, 9N, 18A, 18B, 18F, 19B, 19C, 23A, and 23B), and non-PCV7 serotypes (all others).

Main Results There were 1379 cases of pneumococcal meningitis. The incidence declined from 1.13 cases to 0.79 case per 100 000 persons between 1998–1999 and 2004–2005 (a 30.1% decline, $P < .001$). Among persons younger than 2 years of age and those 65 years of age or older, the incidence decreased during the study period by 64.0% and 54.0%, respectively ($P < .001$ for both groups). Rates of PCV7-serotype meningitis declined from 0.66 case to 0.18 case (a 73.3% decline, $P < .001$) among patients of all ages. Although rates of PCV7-related serotype disease decreased by 32.1% ($P = .08$), rates of non-PCV7-serotype disease increased from 0.32 to 0.51 (an increase of 60.5%, $P < .001$). The percentages of cases from non-PCV7 serotypes 19A, 22F, and 35B each increased significantly during the study period. On average, 27.8% of isolates were nonsusceptible to penicillin, but fewer isolates were nonsusceptible to chloramphenicol (5.7%), meropenem (16.6%), and cefotaxime (11.8%). The proportion of penicillin-nonsusceptible isolates decreased between 1998 and 2003 (from 32.0% to 19.4%, $P = .01$) but increased between 2003 and 2005 (from 19.4% to 30.1%, $P = .03$).

Conclusions Rates of pneumococcal meningitis have decreased among children and adults since PCV7 was introduced. Although the overall effect of the vaccine remains substantial, a recent increase in meningitis caused by non-PCV7 serotypes, including strains nonsusceptible to antibiotics, is a concern.

Commentary Hsu et al report significant reductions of 64% in children < 2 years of age and 54.0% in adults ≥ 65 years old in the overall incidence of pneumococcal meningitis ($P < .001$ for each comparison). For all ages, the rate of disease for the 7 serotypes in the vaccine decreased by 73.3%

($P < .001$), the rate of PCV-7 related serotypes decreased by 32.1 ($P < .08$). However, the rate of non-PCV7 serotypes increased by 60.5% ($P < .001$). The increase in disease caused by non-PCV7 serotypes was primarily accounted for by serotypes 19A, 22F, and 35B, but significant increases also occurred for serotypes 11A and 16F. Although the overall incidence of non-PCV7 meningitis remained low, increasing from only from 0.32 cases to 0.51 cases per 100 000 person-years, the change was most dramatic in children < 2 years of age where the incidence increased from 0.77 to 2.87 cases per 100 000 person-years. Although much attention has been focused in past years on the emergence of serotype 19A after PCV7 introduction, these data demonstrate a more diverse variability of pneumococcal serotype dynamics. Although the increasing numbers of 19A

cases have been primarily antibiotic-resistant clones, this was not the case for other serotypes such as 35B. This indicates that even though antibiotic selection pressure may have played a role in the emergence of serotype 19A, other factors such as vaccine selection pressure or perhaps normal cyclic variability in the incidence of individual serotypes may be behind changes observed for other serotypes. Regardless, the fact that non-vaccine serotypes are causing an increasing amount of disease and that only some of these serotypes are present in newer pneumococcal conjugate vaccines could mean that our battle against this pathogen will be long and complicated.

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