

**Outcomes** Sensitivity, specificity, positive and negative predictive values, and likelihood ratio for pulse oximetry screening and for neonatal physical examination alone.

**Main Results** In West Götaland, 29 babies in well baby nurseries had duct-dependent circulation undetected before neonatal discharge examination. In 13 cases, pulse oximetry showed oxygen saturation  $\leq 90\%$ , and clinical staff were immediately told of the results. Of the remaining 16 cases, physical examination alone detected 10 (63%). Combining physical examination with pulse oximetry screening had a sensitivity of 82.8% (95% CI 64.2% to 95.2%) and detected 100% of the babies with duct-dependent lung circulation. Five cases were missed (all with aortic arch obstruction). The false-positive rate with pulse oximetry was substantially lower than that with physical examination alone (0.17% vs 1.90%,  $P < .0001$ ), and 31/69 of the “false-positive” cases with pulse oximetry had other disease. The risk of leaving the hospital with undiagnosed duct-dependent circulation was 28% in other regions versus 8% in West Götaland ( $P < .0025$ , relative risk 3.36 [95% CI 1.37 to 8.24]). In the other regions, 44% of babies with transposition of the great arteries left hospital undiagnosed versus 0/18 in West Götaland ( $P < .0010$ ), and severe acidosis at diagnosis was more common (33% vs 12%,  $P < .0025$ , relative risk 2.8 [1.3 to 6.0]). Excluding premature babies and Norwood surgery, babies discharged without diagnosis had higher mortality rates than those diagnosed in the hospital (18% vs 0.9%,  $P < .0054$ ). No baby died of undiagnosed duct-dependent circulation in West Götaland versus 5 babies from the other regions.

**Conclusions** Introducing pulse oximetry screening before discharge improved total detection rate of duct-dependent circulation to 92%. Such screening seems cost neutral in the short term, but the probable prevention of neurologic morbidity and reduced need for preoperative neonatal intensive care suggest that such screening will be cost-effective in the long term.

**Commentary** Infants discharged from the birth hospital without identification of their critical congenital heart disease have increased mortality and morbidity rates compared with those who receive a diagnosis; universal neonatal pulse oximetry screening has been introduced as a means to identify a greater proportion of such infants. The authors of this study demonstrated a reduction in the proportion of infants discharged without a diagnosis from 28% (consistent with other data) to 8% with the introduction of screening. Other very large studies have similar results.<sup>1</sup> Saturation in a lower limb  $< 96\%$  obtained from a new-generation motion artefact-resistant oximeter after 20 hours of age, when performed by adequately trained technicians for at least 360 seconds, appears to be a reliable indicator of duct-dependent right-sided heart disease.<sup>2</sup> A gradient of more than 3% between the right hand and a foot may be a useful indicator of left-sided disorders.<sup>2</sup> The 0.17% false-positive rate reported by de-Wahl Granelli et al seems reasonable if it can be reproduced in routine usage, which will be important to minimize the potential harm of parental stress. Even so, screening for a relatively rare

condition will usually result in more false positive than true-positive results, and counselling must take this into account. Screening does not detect all critical congenital heart disease, particularly coarctation of the aorta as these authors again demonstrate, and infants presenting with clinical signs consistent with heart disease must still have consideration of this as a diagnostic possibility, even if previously screened. In 2005, a systematic review labeled pulse oximetry screening “promising”<sup>3</sup>; these new large studies suggest that the promise is being fulfilled.

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## Adjustment of cerebrospinal fluid cell counts for a traumatic lumbar puncture does not aid diagnosis of meningitis in neonates

Greenberg RG, Smith PB, Cotton CM, Moody MA, Clark RH, Benjamin DK. Traumatic lumbar punctures in neonates: test performance of the CSF WBC. *Pediatr Infect Disease J* 2008;27:1047-51.

**Question** Among neonates with suspected meningitis, does the cerebrospinal fluid (CSF) white blood cell count need to be adjusted for a traumatic lumbar puncture?

**Design** Cohort study performed between 1997 and 2004.

**Setting** One hundred fifty neonatal intensive care units in the United States.

**Participants** A total of 6374 neonates  $\leq 30$  days who underwent a lumbar puncture.

**Intervention** CSF white blood cell counts were adjusted downward for traumatic lumbar punctures (defined as CSF specimens with  $\geq 500$  red blood cells/mm<sup>3</sup>) with several commonly used methods.

**Outcomes** Sensitivity, specificity, likelihood ratios, and area under the receiver operating characteristic curve of unadjusted and adjusted CSF white blood cell counts for predicting culture or Gram stain-positive meningitis in neonates with traumatic lumbar punctures.

**Main Results** Of the lumbar punctures, 2519 (39.5%) were traumatic. One hundred fourteen (1.8%) were culture- or Gram stain-positive for meningitis; 50 neonates with traumatic lumbar punctures had meningitis. The areas under

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.<sup>1</sup> 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.<sup>2</sup> 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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## 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  $\geq 65$  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%