cold sore frequency in human subjects [5, 6]. It is important to point out that the apolipoprotein E alleles are on human chromosome 19 at q13.32, rather than chromosome 21, where we identified the region associated with cold sore susceptibility. Our linkage data were conducted in a large, family based, healthy population without prior selection for HSV or Alzheimer disease status. Our genome scan included the polymorphic repeat marker UT7544 (D19S559) that maps ~0.08 Mb from apolipoprotein E. There was no significant linkage between this marker and the HSL phenotypes described in our article. However, the evidence for a role of apolipoprotein E in HSV-1 reactivation disease warrants a closer examination of these alleles in our subjects. This experiment is now in progress.

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References


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Bacteremia Is Associated with a Worse Outcome in Pneumococcal Meningitis

To the Editor—We read with interest the article by Brandt et al. [1] on the impact of bacteremia on pneumococcal meningitis. Data from our clinical cohort of acutely ill Malawian children with pneumococcal meningitis confirms some of their conclusions. We have clinical data on 160 children with pneumococcal meningitis, of whom 36 (22.5%) had no bacteremia. We compared age at presentation, clinical outcome, cerebrospinal fluid (CSF) bacterial load, and Blantyre Coma Score (BCS) on admission [2] and neurological outcome at 6 months between children with bacteremic pneumococcal meningitis and those without.

Children were recruited into the study as part of a larger study examining the cytokine profile of invasive pneumococcal disease [3]. Blood and CSF were collected at admission and analyzed for full blood count, CSF microscopy, and pneumococcal bacterial loads. Coma was defined as a BCS ≤2. The age range was from 0.17 to 14.25 years, (median, 2.13 years), and there were 85 males (53%). A total of 50 children (31%) died, and 77 (48%) had coma. The median CSF bacterial load was significantly higher and the median BCS significantly lower in children with bacteremia than in those without (1.41 × 10⁶ vs. 5.09 × 10⁵ DNA copies/mL [P = .008] and 2 vs. 4 [P = .005], respectively) (figure 1). The median CSF white cell count (WCC) was not significantly different between bacteremic and nonbacteremic pneumococcal meningitis, but blood WCC was significantly higher in children with bacteremic pneumococcal meningitis (18.9 × 10⁹ vs. 10.0 × 10⁹ cells/L; P < .0005). There was no significant correlation between CSF bacterial load and age or CSF WCC, but there was a significant negative correlation between blood WCC and blood

Figure 1. Cerebrospinal fluid (CSF) bacterial load in bacteremic and nonbacteremic pneumococcal meningitis. Box plots represent medians (interior lines), 25th and 75th percentiles (bottom and top edges of boxes), and maximum and minimum values excluding outliers (whiskers).
bacterial load ($r = -0.51; P < .0005$). HIV status was not significantly different between the bacteremic and nonbacteremic groups.

A higher proportion of children with bacteremia had a $\text{BCS} = 2$ than did those without (54% vs. 28%; $P = .006$), and a higher proportion of children with bacteremia died, compared with those without (36% vs. 14%; $P = .01$). Children with bacteremia were significantly younger than those without (7.38 vs. 1.17 years; $P < .0005$). Having a history of antibiotic administration and duration of symptoms did not significantly affect whether there was bacteremic or nonbacteremic meningitis at presentation.

We have previously shown that blood and CSF bacterial loads correlated with outcome and cytokine levels in children with pneumococcal meningitis [3]. Experimental animal models of infection may provide useful new information on disease processes of importance to the human host, but such findings will always need to be confirmed in humans with acute infection, because conditions under controlled experiments are very different from those in real life during a critical illness. The data presented here support the conclusions of Brandt et al. and suggest that, in pneumococcal meningitis, systemic infection is related to more severe disease at presentation, is associated with higher CSF bacterial loads, and tends to occur in younger children.

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References

1. Brandt CT, Holm D, Liptrot M, et al. Impact of bacteremia on the pathogenesis of experimen-