Editors’ Note: Dr. Rosenberg questions whether the resolution of the mild cognitive impairment in the study by Drs. Koepsell and Monsell was not in fact caused by a statistical phenomenon—regression to the mean—which can make natural variation in repeated data look like real change. Regal discusses whether encephalopathy or delirium is the best description for patients with neurologic manifestations of Escherichia coli infection–induced hemolytic-uremic syndrome. Dr. Brouwer responds to Dr. Boelman, who suggests that meningitis-related stroke may confound the outcome difference in pneumococcal and meningococcal meningitis.

Chafic Karam, MD, and Robert C. Griggs, MD

REVERSION FROM MILD COGNITIVE IMPAIRMENT TO NORMAL OR NEAR-NORMAL COGNITION: RISK FACTORS AND PROGNOSIS

Gilad Rosenberg, Jerusalem: Drs. Koepsell and Monsell analyzed a population of subjects with mild cognitive impairment (MCI) who allegedly reverted back to normal cognition, only to remain at a high risk of subsequently progressing to Alzheimer disease.1 Out of 3,020 subjects diagnosed with MCI at their initial study visit, the authors’ analysis focused on a subgroup of 483 subjects who—1 year later—had no MCI.

Regression to the mean is a statistical phenomenon that can make natural variation in repeated data look like real change.2 Is it possible that the observed reversion from MCI was in fact regression to the mean?

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NEUROLOGIC MANIFESTATIONS OF E COLI INFECTION-INDUCED HEMOLYTIC-UREMIC SYNDROME IN ADULTS

Paul J. Regal, Lake Haven, Australia: I commend Weissenborn et al.1 for careful serial neurologic and neuropsychological examination of 42 severely ill adults. I question whether encephalopathy or delirium is the best description. The first of 2 cardinal features of delirium on the Confusion Assessment Method (CAM)2 is acute confusion with fluctuating course. All the observations support sudden onset. The low median age of 43 years makes prior brain disease such as Alzheimer disease and stroke unlikely in most subjects. Figure 2 demonstrates great fluctuation in neuropsychological dysfunction.1 The second CAM cardinal feature is inattention. Twenty-one patients had impaired working memory. We can safely infer that almost all 21 had inattention; 10 patients with stupor or coma had inattention. Thus the first 2 cardinal features of delirium were fulfilled in an estimated 30 patients. CAM positivity requires disorganized thinking or altered level of consciousness. Ten had altered level of consciousness and many of the 24 patients whose Mini-Mental State Examination fell below 28 or the 5 who developed agitation would likely have disorganized thinking. I estimate 50% of these patients had CAM-positive delirium. In 584 key articles on delirium, this is the first report of delirium in adults with hemolytic uremic syndrome.

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ADJUNCTIVE DEXAMETHASONE IN ADULTS WITH MENINGOCOCCAL MENINGITIS

Cyrus G. Boelman, Toronto: In the article by Heckenberg et al.,1 the authors conclude that dexamethasone did not similarly improve the unfavorable outcome in meningococcal meningitis as was seen in their previous pneumococcal cohort study.2 The difference in the incidence of meningitis-related stroke between these meningitis populations may explain the difference in the cohorts’ Glasgow Outcome Scale results.

Stroke occurs more commonly in pneumococcal meningitis. Brouwer et al.2 reported infarction in 7% of the 90% of patients who received a cranial CT on
hospital admission. In the current meningococcal study, a single patient (1.5%) had an infarction on imaging on admission, yet only 6.9% of patients were imaged.1

No further stroke data are provided; however, the “focal cerebral deficits” likely include symptomatic strokes. The meningococcal study had 12% of patients with focal deficits in both treatment populations on admission and only 4% and 2% on discharge in the dexamethasone and nondexamethasone groups, respectively. In contrast, the pneumococcal study had focal deficits on discharge in 11% of both treatment groups.

The authors did not discuss how dexamethasone was associated with stroke incidence. Dexamethasone cannot be expected to reduce overall morbidity in meningococcal meningitis if it acts to reduce stroke morbidity. Future studies of bacterial meningitis should highlight the incidence of stroke in these populations.

Author Response: Matthijs C. Brouwer, Diederik van de Beek, Amsterdam: Cerebral infarction is a severe complication in bacterial meningitis and is particularly common in pneumococcal meningitis. Severity of CNS inflammation is related to the risk of cerebral infarction.3

A randomized study in adults with bacterial meningitis showed that adjunctive treatment with dexamethasone reduced the risk of unfavorable outcome.4 The benefit of dexamethasone was greatest in patients with pneumococcal meningitis, in whom mortality was reduced from 34% to 14%. Interestingly, the survival benefit of dexamethasone in pneumococcal meningitis was a result of reduced mortality from systemic causes, and not neurologic causes.5

In our implementation study, we observed a decreased rate of cerebral infarctions in pneumococcal meningitis after the implementation of dexamethasone, from 36% to 29% (p = 0.04).2 For meningococcal meningitis, we found a nonsignificant decreased infarction rate after the implementation of dexamethasone (9% vs 5%; p = 0.36).1

Pneumococcal meningitis is more severe than meningococcal meningitis, with higher rates of complications including sepsis, cerebrovascular complications, epilepsy, hydrocephalus, and hearing loss.2,4 A potential difference in the efficacy of dexamethasone between pathogens can be partially explained by differences in stroke ratio between patients with meningococcal and pneumococcal meningitis.

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Adjunctive dexamethasone in adults with meningococcal meningitis
Cyrus G. Boelman, Matthijs C. Brouwer and Diederik van de Beek
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