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?

© 2013 American Academy of Neurology

1. Koepsell TD, Monsell SE. Reversion from mild cognitive impairment to normal or near-normal cognition: risk factors and prognosis. *Neurology* 2012;79:1591–1598.
2. Barnett AG, van der Pols JC, Dobson AJ. Regression to the mean: what it is and how to deal with it. *Int J Epidemiol* 2005;34:215–220.

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.

© 2013 American Academy of Neurology

1. Weissenborn K, Donnerstag F, Kielstein JT, et al. Neurologic manifestations of *E coli* infection-induced hemolytic uremic syndrome in adults. *Neurology* 2012;79:1466–1473.
2. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegel AP, Horwitz RI. Clarifying confusion: the confusion assessment method: a new method for detection of delirium. *Ann Intern Med* 1990;113:941–948.

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.

© 2013 American Academy of Neurology

1. Heckenberg SGB, Brouwer MC, van der Ende A, van de Beek D. Adjunctive dexamethasone in adults with meningococcal meningitis. *Neurology* 2012;79:1563–1569.
2. Brouwer MC, Heckenberg SGB, de Gans J, Spanjaard L, Reitsma JB, van de Beek D. Nationwide implementation of adjunctive dexamethasone therapy for pneumococcal meningitis. *Neurology* 2010;75:1533–1539.
3. Vergouwen MD, Schut ES, Troost D, van de Beek D. Diffuse cerebral intravascular coagulation and cerebral infarction in pneumococcal meningitis. *Neurocrit Care* 2010;13:217–227.
4. de Gans J, van de Beek D. Dexamethasone in adults with bacterial meningitis. *N Engl J Med* 2002;347:1549–1556.
5. van de Beek D, de Gans J. Dexamethasone and pneumococcal meningitis. *Ann Intern Med* 2004;141:327.

Neurology® WriteClick: Join the Debate!

The editors encourage comments about recent articles through WriteClick:

Go to www.neurology.org and click on the “WriteClick” tab at the top of the page. Responses will be posted within 72 hours of submission.

Before using WriteClick, remember the following:

- WriteClick is restricted to comments about studies published in *Neurology* within the last eight weeks
- Read previously posted comments; redundant comments will not be posted
- Your submission must be 200 words or less and have a maximum of five references; reference one must be the article on which you are commenting
- You can include a maximum of five authors (including yourself)

Author disclosures are available upon request (journal@neurology.org).

Neurology®

Adjunctive dexamethasone in adults with meningococcal meningitis

Cyrus G. Boelman, Matthijs C. Brouwer and Diederik van de Beek

Neurology 2013;80;1818-1819

DOI 10.1212/01.wnl.0000430451.92743.a5

This information is current as of May 6, 2013

Updated Information & Services

including high resolution figures, can be found at:
<http://n.neurology.org/content/80/19/1818.3.full>

References

This article cites 5 articles, 2 of which you can access for free at:
<http://n.neurology.org/content/80/19/1818.3.full#ref-list-1>

Permissions & Licensing

Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
http://www.neurology.org/about/about_the_journal#permissions

Reprints

Information about ordering reprints can be found online:
<http://n.neurology.org/subscribers/advertise>

Neurology® is the official journal of the American Academy of Neurology. Published continuously since 1951, it is now a weekly with 48 issues per year. Copyright © 2013 American Academy of Neurology. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.