to significant reductions in depression. It remains to be seen where riluzole will ultimately land in our armamentarium, but it too is promising.

J. C. Ballenger, MD

Antidepressant Efficacy of the Antimuscarinic Drug Scopolamine: A Randomized, Placebo-Controlled Clinical Trial

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Context.—The need for improved therapeutic agents that more quickly and effectively treat depression is critical. In a pilot study we evaluated the role of the cholinergic system in cognitive symptoms of depression and unexpectedly observed rapid reductions in depression severity following the administration of the antimuscarinic drug scopolamine hydrobromide (4 μg/kg intravenously) compared with placebo ($P=.002$). Subsequently a clinical trial was designed to assess more specifically the antidepressant efficacy of scopolamine.

Objective.—To evaluate scopolamine as a potential antidepressant agent.

Design.—Two studies were conducted: a double-blind, placebo-controlled, dose-finding study followed by a double-blind, placebo-controlled, crossover clinical trial.

Setting.—The National Institute of Mental Health.

Patients.—Currently depressed outpatients aged 18 to 50 years meeting *DSM-IV* criteria for recurrent major depressive disorder or bipolar disorder. Of 39 eligible patients, 19 were randomized and 18 completed the trial.

Interventions.—Multiple sessions including intravenous infusions of placebo or scopolamine hydrobromide (4 μg/kg). Individuals were randomized to a placebo/scopolamine or scopolamine/placebo sequence (series of 3 placebo sessions and series of 3 scopolamine sessions). Sessions occurred 3 to 5 days apart.

Main Outcome Measures.—Psychiatric evaluations using the Montgomery-Asberg Depression Rating Scale and the Hamilton Anxiety Rating Scale were performed to assess antidepressant and antianxiety responses to scopolamine.

Results.—The placebo/scopolamine group showed no significant change during placebo infusion vs baseline; reductions in depression and anxiety rating scale scores ($P<.001$ for both) were observed after the administration of scopolamine compared with placebo. The scopolamine/placebo group also showed reductions in depression and anxiety rating scale scores ($P<.001$ for both) after the administration of scopolamine, relative to baseline, and these effects persisted as they received placebo. In both groups, improvement was significant at the first evaluation after scopolamine administration ($P\leq.002$).

Conclusion.—Rapid, robust antidepressant responses to the antimuscarinic scopolamine occurred in currently depressed patients who predominantly had poor prognoses.

► This trial is an example of a frequent issue seen in the evolution of treatment advances. These authors studied the antimuscarinic drug scopolamine in depressed and generally treatment-resistant patients at the NIMH. I can remember 30 years ago David Jimerson at the NIMH hypothesizing and finding positive effects with other antimuscarinic agents in depressed patients. However, this hypothesis was not in sync with much of the evolving monamine thinking in depression at the time, was hard to administer, and was associated with significant side effects. However, David did find positive effects. This group now has definitively demonstrated that IV administration of scopolamine had persisting antidepressant responses. I hope this lead will not be lost again. Part of what may keep this going, although it is hard to see an obvious commercial development, is that the effects that were observed were very rapid. This IV treatment could well become an inpatient treatment of depression.

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Do essential fatty acids have a role in the treatment of depression?
Williams A, Katz D, Ali A, et al (Yale Prevention Research Ctr, Derby, Conn; Yale Univ School of Nursing; Yale Univ School of Medicine; et al)
J Affect Disord 93:117-123, 2006

Background.—Complementary and alternative medicine (CAM) therapies are used more than conventional therapies by people with self-defined anxiety and depression. Preliminary evidence supports a hypothesis that low plasma concentration of essential fatty acids is associated with depression. Reported here is the result of a systematic review examining the therapeutic efficacy of essential fatty acids for depression.

Methods.—Data sources included Medline, Psychinfo, AMED (Allied and Complementary Medicine), and Cochrane Controlled Trials Register databases searched from inception through September 2001. English language randomized controlled trials, controlled clinical trials, intervention studies, case control studies, reviews, and case reports of humans were selected, without limits for demographics or co-morbidities. Two abstractors independently evaluated each study, then reconciled findings. When possible, between group treatment effect size was noted or calculated.

Results.—Six articles met inclusion criteria: one RCT, two reviews, and three case control trials. A common outcome measure among the case control trials allowed for direct comparison of effect sizes.

Conclusions.—The evidence implies promise of a treatment effect of omega-3 fatty acids for depression in adults; although a statement of definitive clinical efficacy is premature. Further study of essential fatty acids as independent and adjuvant therapy for adult depression is indicated, including more sophisticated investigation of dose-response in particular populations.

► The authors have analyzed the existing published literature and suggest that the answer to the question in the title is that, although a definite state-