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IN THIS ISSUE

Focus of the Month:
The Diagnosis and Treatment of Dementia

Medications for Treating Alzheimer's Dementia

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Dr. Shah, Dr. Threlfall and Lynn Shell have disclosed that they have no relevant relationships or financial interests in any commercial company pertaining to this educational activity.

While drug companies have been working hard to come up with new options for the treatment of dementia, there have been no new FDA approvals since memantine (Namenda) hit the scene in 2003. The currently available meds include four cholinesterase inhibitors (donepezil, galantamine, rivastigmine and tacrine) and one NMDA receptor antagonist (memantine). Frankly, they have only modest efficacy, but these are the only pharmacological tools we have—so let's review their clinical utility.

Before starting, however, there is an important point to be made about the nature of the clinical trial evidence. Although these medications can sometimes temporarily improve the symptoms of dementia, they usually work by modestly slowing the decline of cognition. It is important to explain this point to family members, who might otherwise expect to see actual improvement in cognition, which is unusual.

Cholinesterase Inhibitors

Remembering how cholinesterase inhibitors (CIs) work is helpful in remembering their side effects. Acetylcholine, one of the neurotransmitters involved with memory, is inactivated by the enzyme acetylcholinesterase. The four CIs work by blocking the acetylcholinesterase and increasing acetylcholine in the synaptic cleft—leading to the nasty side effects of nausea, vomiting and dizziness that we find with these medications. In addition, tacrine (Cognex) can cause hepatotoxicity, and is so rarely used that we won't discuss it in detail.

All three of the commonly used CIs perform equally well, according to a meta-analysis of 13 randomized double blind placebo-controlled trials (Birks J., Cholinesterase inhibitors for Alzheimer's Disease. *Cochrane Database of Systematic Reviews* 2006).

Donepezil (Aricept) is generally well tolerated, easy to dose and has an added bonus in that it is the only CI that is FDA approved to treat severe dementia as well as mild to moderate dementia. Start at 5 mg every morning and go up to 10 mg after four weeks. Dosing it in the morning may prevent the side effect of insomnia and vivid dreams some patients report on the medication. According to the Cochrane Review, donepezil causes fewer side effects than rivastigmine.

Galantamine (Razadyne) comes in both immediate-release tablets (with

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Learning objectives for this issue: 1. Classify the medications used to treat Alzheimer's dementia and their side effects. **2.** Describe scales used to monitor dementia symptoms and the applications of each. **3.** Identify some neuroimaging tools used in diagnosing dementia. **4.** Understand the most current findings in the literature regarding psychiatric treatment. This CME/CE activity is intended for psychiatrists, psychiatric nurses, psychologists and other health care professionals with an interest in the diagnosis and treatment of psychiatric disorders.

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initial dosing starting at 4 mg twice a day), or an extended-release tablet (an initial dose of 8 mg once a day). The dose can be increased every four weeks to a maximum of 24 mg per day. Galantamine's original boast was that it has a dual mechanism of action, working on nicotinic receptors as well. However, accumulating evidence seems to show that this does not make any difference in efficacy (Loy C et al., Galantamine in Alzheimer's Disease. *Cochrane Database of Systematic Reviews* 2002. Updated 2006). One piece of bad news is that galantamine may cause a slightly higher mortality rate than placebo when given off-label to patients with mild cognitive impairment (*ibid*).

Both donepezil and galantamine are substrates of CYP2D6 and CYP3A4, so medications that inhibit these enzymes (such as some SSRIs and duloxetine) can increase levels of both CIs, potentially worsening side effects.

Rivastigmine (Exelon), indicated for mild to moderate AD, is the only CI FDA-approved to treat dementia associated with Parkinson's disease. Unfortunately, the oral form causes particularly high rates of nausea, vomiting, weight loss and syncope, and the titration to higher doses is difficult for many patients to tolerate (Birks J et al., Rivastigmine for Alzheimer's Disease. *Cochrane Database of Systematic Reviews* 2000. Updated 2009). The good news is that rivastigmine is now offered in a transdermal patch which is better tolerated. The target dose of the patch is 9.5 mg per 24 hours, which is similar to oral dose of 6 mg twice a day. Start with a 4.6 mg per 24 hours patch for four weeks and then move up to the 9.5 mg per 24 hours patch. Unlike donepezil and galantamine, rivastigmine is not metabolized by the liver and therefore presents little risk of drug interactions.

Since all of the CIs are equally effective, we recommend starting with donepezil, given its once a day dosing and good tolerability profile. Donepezil will soon be available in a cheaper generic form (probably by the end of 2010).

The perpetually vexing issue in dementia treatment is how long to continue CIs once you've started. Most consensus guidelines recommend trying another CI if there is no clear slowing of cognitive decline in the first six to nine months, although the research on this is sparse (Tariot P et al., *J Clin Psychiatry* 2006;67(suppl 3):2002–2013). Most experts believe that you can switch from one CI to another without a washout period, but there is one case report of a fatal adverse event during a transition from donepezil to rivastigmine. (For a review of the literature on this topic, see Burns A et al., *J Psychopharmaco* 2006; 20(6):732–755.)

Memantine

Memantine (Namenda), the fifth medication used to treat AD, is an N-methyl-D-aspartate (NMDA) receptor antagonist, and may work by slowing the activation of NMDA receptors caused by excessive glutamate release.

Memantine is FDA-approved for the treatment of moderate to severe AD only, and a 2006 Cochrane Review showed that it has a small beneficial effect on both cognition and behavior after six months in such patients (McShane R et al., Memantine for Dementia. *Cochrane Database of Systematic Reviews* 2005. Updated 2006). Memantine may also be effective as an augmentation agent added to donepezil in patients with moderate to severe AD. One large randomized, placebo-controlled study of 404 patients with moderate to severe AD showed significant but modest improvements in cognition, activities of daily living, and behavior in those receiving donepezil and memantine as compared to those receiving donepezil and placebo. Confusion was the most common adverse event attributable to memantine (7.9% on memantine vs 2.0% on placebo; P = .01) (Tariot et al., *JAMA* 2004;(3)291: 317–324).

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Medications for Alzheimer's Dementia

Medication	FDA Indications	Available Strengths	Starting Dose	Target Dose	Common Side Effects
Aricept (donepezil)	Mild to severe AD	5 mg, 10 mg	5 mg Q am	10 mg Q am	Nausea, diarrhea, insomnia and fatigue. Morning dosing may prevent insomnia and vivid dreams.
Razadyne (galantamine)	Mild to moderate AD	4 mg, 8 mg, 12 mg (immediate release); 8 mg, 16 mg, 24 mg (extended release)	4 mg BID (for immediate release formula) or 8 mg QD (for extended release formula)	Max of 24 mg QD	Nausea, vomiting, diarrhea, and stomach upset. Side effects may be reduced if taken with food.
Exelon (rivastigmine)	Mild to moderate AD, dementia of PD	1.5 mg, 3 mg, 4.5 mg, 6 mg capsules; 2 mg/ml liquid	1.5 mg BID	6 mg BID	Nausea, vomiting, weight loss and syncope. Reputed to have the worst side effects of all the CIs.
Exelon transdermal patch	Mild to moderate AD	4.6 mg per 24 hours, 9.5 mg per 24 hours	4.6 mg per 24 hours	9.5 mg per 24 hours	Nausea, dizziness and drowsiness. More tolerable than oral Exelon.
Namenda (memantine)	moderate to severe AD	5 mg, 10 mg tablets; 2 mg/ml liquid	5 mg QD	10 mg BID	Dizziness, sedation, transient confusion.

AD = Alzheimer's dementia; PD = Parkinson's disease
Tacrine, while FDA-approved for dementia, is not included in this chart because it is rarely used due to hepatoxicity.
None of the listed medications are available in generic form, though Aricept is expected to go generic by the end of 2010.

Medications for Treating Alzheimer's Dementia

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We recommend adding memantine when dementia has progressed to the moderate or severe level. Usual dosing starts at 5 mg per day for the first week, 5 mg twice a day for the second week, 10 mg in the morning and 5 mg at bedtime for the third week, and a final increase to 10 mg twice a day in the fourth week. A recent study showed that switching from donepezil to memantine (for reasons of tolerability or functional decline) can be done safely either abruptly or through cross titration (Waldemar et al., *Int Jrn of Geriatric Psychiatry* 2008;23(9):979-981).

Another pressing question is whether these medications work for agitation or behavioral issues in dementia patients. While atypical antipsychotics are often used for agitation, they are associated with a small excess risk of mortality and are best used sparingly. Recently, some retrospective pooled analyses have shown that memantine can be helpful for agitation and aggression in AD. But these are not clinical trials, and are therefore less compelling. (For recent research, see Wilcock GK et al., *J Clin Psychiatry* 2008;69(3):341–348.) The only clinical trial of a CI for agitation was negative: a 2007 study of 272 patients with AD randomly assigned to either donepezil or placebo showed no significant differences between the two for behavioral symptoms (Howard RJ et al., *N Eng J Med* 2007; 357(14) 1382–1392).

TCPR'S VERDICT: ***Start with Aricept, add Namenda if needed.***

Monitoring Dementia Symptoms: Which Scales are Practical for Clinicians?

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Let's assume that you have already diagnosed a patient with Alzheimer's Disease (AD). Your patient has received a full workup to rule out medical causes, and has had a full battery of neuropsychological tests. (See this month's interview with Dr. Small for guidance on this initial workup.) Let's further assume that you have started a standard cocktail of whichever cholinesterase inhibitor you prefer, plus memantine (Namenda).

Actually, that was the easy part. Now, you have to figure out if the medications are working. You're dissatisfied with the old fashioned method of simply asking the patient and the family if there has been any improvement or decline in functioning, because it is too subjective. You'd like to be able to get a number to write in the chart so that you can convincingly demonstrate that treatment is working (or not).

The standard research instrument used for monitoring treatment outcomes in dementia is the Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-Cog) (Rosen WG et al., *Am J Psychiatry* 1984;141(11):1356–64). While it is useful in research, the ADAS-Cog takes 30 minutes to administer and is thus too time consuming for the average busy clinician.

Two common alternatives that have been brought over from the bench to the bedside are the Mini Mental State Exam (MMSE) (Folstein MF et al., *J Psychiatr Res* 1975;12:189–198) and the Clock Drawing Test (Sunderland T et al., *J Am Geriatr Soc* 1989;37(8):725-729). The MMSE is quick—usually completed in less than 10 minutes—and effective at identifying and monitoring moderate to severe dementia. Studies have documented a typical decline of two to four points over 12 months if dementia is untreated. For patients who have been treated, the decline in scores is generally no more than one point (Winblad B et al., *Neurology* 2001;57:489–495; Courtney C et al., *Lancet* 2004;363:2105–2115). Keep in mind, however, that the test is not sensitive for mild cognitive impairment (MCI) or mild AD (Ihl R et al., *Psychiatry Res* 1992;44:93–106; Tombaugh TN et al., *J Am Geriatr Soc* 1992;40: 922–935), or for detecting impairment in patients who are well-educated and intelligent (Crum RM et al., *JAMA* 1993;269:2386–2391).

A relatively new test, called the Mini-Cog (Borson J et al., *J Am Geriatr Soc* 2003;51(10):1451–1454), is a combination of the MMSE's three item recall question and the Clock Drawing Test. The Mini-Cog is administered in two steps. First, you ask your patient to repeat and memorize three simple words (the specific words are up to you). Then you give him a paper and pen, and ask him to draw a clock with the hands pointing to "11:10." Once the clock is drawn, ask him to repeat your three words. The Mini-Cog is faster to administer than the MMSE, and studies have shown no significant differences in sensitivity or specificity between the two.

In measuring cognition on the milder end of the spectrum (MCI and mild AD), a potential alternative to the MMSE and the Mini-Cog is the Montreal Cognitive Assessment (MoCA). The MoCA emphasizes language and executive skills, takes about 10 minutes to conduct, and is very effective for identifying MCI (Nasreddine ZS et al., *J Am Geriatr Soc* 2005;53:695–699). The MoCA test and instructions are available for free at www.mocatest.org. (For *TCPR*'s take on the MoCA, see "The MoCA: A Better MMSE?" *TCPR* May 2008.)

While these instruments are effective in assessing cognition, they neglect some

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Q&A With the Expert

This Month's Expert

Neuroimaging and Other Diagnostic Tools for Dementia

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Dr. Small has disclosed that he has no relevant relationships or financial interests in any commercial company pertaining to this educational activity.

TCPR: As a neurologist, how do you approach the evaluation of dementia symptoms?

Dr. Small: I think of the causes as fitting into four categories: toxic/metabolic, structural lesions, psychiatric illness or neurodegeneration.

TCPR: How do you go about evaluating these possibilities?

Dr. Small: To rule out toxic metabolic causes of dementia, I will typically check a B12, folate, thyroid levels and RPR [rapid plasma reagin test for syphilis]. If there is something in the clinical picture that makes me worry about Lyme disease, liver toxicity or HIV, I will test for those as well.

TCPR: How do you assess for structural lesions?

Dr. Small: I'll typically order a structural MRI or a CAT scan if I suspect structural lesions. I'm looking for anything in the brain that ought not be there and might be compressing or damaging areas involved with cognition. Generally, tumors, large strokes and hydrocephalus are picked up on a good neuro exam, so what I'm really looking for on these imaging tests are small to moderate strokes. Stroke is extremely common, and often people have silent strokes, and this is something we can see well with structural MRI.

TCPR: How do you test for neurodegeneration?

Dr. Small: Neurodegeneration includes the most common causes of dementia, and these have no real diagnostic test. We make the diagnosis by excluding the other categories I mentioned. Once we have determined that the cause of dementia is neurodegeneration, we have to sort through all the types—not only Alzheimer's (which is by far the most common), but Lewy Body degeneration or frontotemporal degeneration, both of which commonly present with psychiatric symptoms.

TCPR: How do you determine which type of neurodegeneration you're looking at?

Dr. Small: We try to identify what areas of the brain are most affected, because although they share some pathogenic background, these disorders are fundamentally different in the areas of the brain they target. So, for example, Alzheimer's disease starts in the hippocampus, and the main characteristic of hippocampal-dependent memory loss is difficulty in encoding new information, not retrieving old information. The typical patient with Alzheimer's can't remember what happened yesterday but has an easy time talking about events that happened years ago. Of course, the most helpful way to identify the areas of the brain involved in memory loss is still brain mapping.

TCPR: And what is the best method of brain mapping?

Dr. Small: The most time-honored technique is neuropsychology. A very skilled neuropsychologist will take three or four hours in order to "interrogate" different parts of the brain, much like an engineer approaches a broken machine.

TCPR: What valuable information do you typically obtain from neuropsychology testing results?

Dr. Small: First, it helps us determine if a patient's cognitive impairment is just normal aging, and second, it can identify a *pattern* of impairment. Although it is rarely clear cut, such testing might show a pattern more consistent with a medial temporal lobe problem or the posterior cortex, for example.

TCPR: When do you turn to neuroimaging such as functional MRI?

Dr. Small: Functional MRI (fMRI) is similar to positron emission tomography (PET) in that it allows us to measure neural activity in different parts of the brain. Although neither technique can actually diagnose dementia, I still use them and I think a lot of clinicians do. If I see severe atrophy in the medial temporal lobes, for example, and I was teetering on the edge of an Alzheimer's diagnosis, this information is very useful.

TCPR: Can you give us another example of when you might use neuroimaging for diagnosis?

Dr. Small: A good example is for a patient who may have Alzheimer's or frontotemporal dementia (FTD). We'll order a PET or SPECT study because these types of neurodegeneration show different patterns. If it's FTD, we'll see lower metabolism in the frontal lobe area. And because the frontal lobes are affected, these patients have behavioral problems—such as violence or mood swings. These are not things you see early on in Alzheimer's disease.

TCPR: So if you are able to determine from an imaging test that a patient has FTD, what does that do for the patient?

Dr. Small: Unfortunately, it really only helps by suggesting the right diagnosis. There is no treatment for FTD. We are able to inform the family what to expect and how to manage it, but we can't give medication or anything curative.

TCPR: What does the future of neuroimaging hold for dementia?

Dr. Small: Researchers are trying to develop variants of high-resolution fMRI that look at the first areas of the brain that are affected by Alzheimer's. With fMRI, SPECT and PET, the goal is to detect cell thickness early on. Right now they're testing PET scans using an imaging agent called PIB—Pittsburgh compound B. This compound can identify plaques and tangles in the brain. It's still in the research phase, but it's very exciting to think we may be able to identify the precursors to Alzheimer's disease before a patient has obvious symptoms. These new technologies may actually someday allow us to diagnose Alzheimer's early.

TCPR: Thank you, Dr. Small.

Monitoring Dementia Symptoms: Which Scales are Practical for Clinicians?

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important aspects of treatment outcome in dementia, particularly caregiver burden and quality of life. Caregiver burden refers to the challenges faced by family members of patients with dementia, and can lead to significant problems with burnout and depression in those who care for such patients (Black W et al., *Int Psychogeriatr* 2004;16(3):295–315). To assess this, we recommend the shortened 7-item Screen For Caregiver Burden available in Appendix 1 at the end of the developer's article (Hirschman KE et al., *JAGS* 2004;52(10):1724–1729).

To assess your patients' quality of life and functional abilities, we recommend the Quality of Life in Alzheimer's Disease scale (QOL-AD) (Logsdon RG et al., *Psychosomatic Medicine* 2002:64: 510–519), which takes about 10 minutes to administer and is available online with instructions at http://bit.ly/9RjySn.

Dementia Scales can help guide our treatment.

Practical Scales for Monitoring Dementia

Scale	What Does It Measure	Notes
Mini Mental State Exam (MMSE)	Cognitive function	Not sensitive for mild impairment
Mini-Cog	Cognitive function	Combines MMSE 3-item recall test with clock drawing test
Montreal Cognitive Assessment (MoCA)	Cognitive function	Can identify mild cognitive impairment
7-item Screen for Caregiver Burden	Caregiver burnout/depression	Shortened version of the Screen for Caregiver Burden
Quality of Life in Alzheimer's Disease scale (QOL-AD)	Functional abilities	Takes 10 minutes to administer

For references, see accompanying article.

Research Updates IN PSYCHIATRY

Section Editor, Glen Spielmans, PhD

Glen Spielmans, PhD has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this article.

PSYCHOSIS

Can Omega 3s Prevent Psychotic Disorders?

Omega 3 fatty acids were once thought to be a possible treatment for mood disorders—but recent studies have been unimpressive. (See *TCPR* February 2010 for a review of omega 3 for depression.) In the latest test of the supplement's psychiatric potential, researchers in Austria used it to prevent the onset of psychosis in high risk young adults.

Eighty-one patients between the ages of 13 and 25 at the outpatient psychosis detection unit of a large public hospital in Vienna were enrolled in this double-blind, placebo-controlled study. All participants in the study were considered at "ultra high risk" of psychotic disorder because they met at least one of three criteria: attenuated psychotic symptoms, transient psychosis, or "trait plus state" risk factors, defined as having a schizotypal personality disorder or a first degree relative with a psychotic disorder, and a decrease in functioning within the past year. Patients were randomized to 12 weeks of either 1.2 g/day of omega 3 or placebo. They were assessed for psychotic symptoms at four, eight, and 12 weeks, and then at six months and 12 months.

One year after the start of the study (and nine months after the treatment was discontinued) 11 of 40 patients (27.5%) who had taken placebo developed a psychotic disorder, as opposed to only two of 41 patients (4.9%) who were assigned to omega 3, a statistically significant difference. Most of those who converted to psychosis were diagnosed with either schizophrenia or schizophreniform disorder. The number needed to treat (NNT) with omega 3 to prevent one person from converting to psychosis was an impressively low four. The treatment was well tolerated, with no significant side effect differences between omega 3 and placebo (Amminger GP et al., *Arch Gen Psychiatry* 2010;67(2):146–154).

TCPR's Take: If these results hold up in future studies, it would imply that omega 3 fatty acids are actually more effective than antipsychotic medication for prevention of psychosis. The sample size was fairly small (though large compared to many prior studies of psychosis prevention), and the included patients were carefully selected, both of which limit the generalizability of the results. But given that the treatment had no side effects, it seems reasonable to try it in pre-psychotic patients, or even as an adjunctive treatment in schizophrenia.

BIPOLAR DEPRESSION

Antidepressants May Not Induce Mania in Bipolar Disorder

The frequency of antidepressant-induced mania has been elusive, with some studies finding high rates of manic switching and others finding very few or no manic episodes among patients taking antidepressants. A recent review sorted through this mixed bag of studies, examining the extent to which antidepressants induce mania or hypomania in both bipolar and unipolar depressed patients.

The authors performed a thorough literature search and included 30 randomized, placebo-controlled trials and 18 open trials in their analyses. The mean follow-up time was about five months. In patients with bipolar disorder, antidepressant use was associated with a slightly higher rate of mania or hypomania—15.3% on ADs vs. 13.8% not on ADs, but this difference was not statistically significant. Surprisingly, the use of mood stabilizers had no effect on the rate of antidepressant-related manic episodes. In patients with major depression, ADs led to a 6% switch rate, significantly greater than the 1.2% switch rate in patients not on ADs.

Risk of switching was higher for patients on tricyclics than SSRIs, though the difference was not statistically significant (Tondo L et al., *Acta Psychiatr Scand* online ahead of print).

TCPR's Take: This study suggests that patients with bipolar disorder have a high risk of becoming manic or hypomanic over an average five month follow-up, but that the use of antidepressants does not increase the switch rate. The story is different in unipolar depression, in which antidepressants yield about a five-fold higher risk of manic/hypomanic switching. But before we conclude that antidepressants are perfectly safe in bipolar disorder, it is important to note that this is only one meta-analysis, and that other studies have reported that antidepressants can worsen the course of bipolar disorder. The authors of the meta-analysis themselves cautioned that the methodology of the included studies was flawed in many cases. Nonetheless, the findings should serve to increase our comfort level in prescribing antidepressants in bipolar depression.

OCD

D-Amphetamine or Caffeine May be Effective Augmentation of SSRIs for OCD

Previous research has shown that a single dose of d-amphetamine 30 mg (as monotherapy) relieves symptoms of OCD better than a placebo (Insel TR et al., *Psychopharmacology* 1983;80:231–235; Joffe RT et al., *J Clin Psychopharmacol* 1991;11:237–241).

In a new report, researchers sought to replicate these findings. They enrolled 24 patients with OCD who had residual symptoms even after at least 12 weeks on an SSRI or SNRI. All patients were randomly assigned to double blind treatment with either 30 mg/day of d-amphetamine or 300 mg/day of caffeine (in a pill that looked identical to the amphetamine, and was intended to be a placebo), in addition to their SSRIs/SNRIs, which they continued. While the trial lasted five

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CME Post-Test

To earn CME or CE credit, you must read the articles and log on to www.TheCarlatReport.com to take the post-test. Please see the study guide listed below to prepare for this month's post–test. Learning objectives are noted on page 1. You must answer at least four questions correctly to earn credit. You will be given two attempts to pass the test. Tests must be taken by March 31, 2011.

As a subscriber to *TCPR,* you already have a username and password to log on to www.TheCarlatReport.com. To obtain your username and password, please email CME@thecarlatreport.com or call 978-499-0583.

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Below are the questions for this month's CME post-test. This page is intended as a study guide. Please complete the test online at www.TheCarlatReport.com. Note: Learning objectives are listed on page 1.

1. The only cholinesterase inhibitor FDA-approved to treat severe dementia is (L.O. #1):
   [[a. Cognex (tacrine)
   [ ] b. Aricept (donepezil)
   [ ] c. Razadyne (galantamine)
   [ ] d. Exelon (rivastigmine)

2. The Mini Mental State Exam (MMSE) is effective at identifying and monitoring moderate to severe dementia, but is not sensitive for mild cognitive impairment (MCI) or mild AD (L.O. #2).
   [ ] a. True
   [ ] b. False

3. The maximum recommended target dose for Razadyne (galantamine) is (L.O. #1):
   [ ] a. 8 mg QD
   [ ] b. 8 mg BID
   [ ] c. 24 mg QD
   [ ] d. 24 mg BID

4. According to Dr. Scott Small, brain mapping helps doctors determine what type of neurodegeneration a patient has (L.O. #3).
   [ ] a. True
   [ ] b. False

5. In the Amminger study, one year after the study began how many of the patients who had been given omega 3 developed a psychotic disorder (L.O. #4)?
   [ ] a. 25 of 41 (61%)
   [ ] b. 11 of 41 (26.8%)
   [ ] c. 4 of 41 (9.8%)
   [ ] d. 2 of 41 (4.9%)

PLEASE NOTE: WE CAN AWARD CME CREDIT ONLY TO PAID SUBSCRIBERS

First Name _____ Last Name _____ Degree (MD, PhD, NP, etc.) _____

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Your evaluation of this CME/CE activity (i.e., this issue) will help guide future planning. Please respond to the following questions:

1. Did the content of this activity meet the stated learning objectives? L.O.#1: [ ] Yes [ ] No L.O.#2: [ ] Yes [ ] No L.O.#3: [ ] Yes [ ] No L.O.#4: [ ] Yes [ ] No
2. On a scale of 1 to 5, with 5 being the highest, how do you rank the overall quality of this educational activity? [ ] 5 [ ] 4 [ ] 3 [ ] 2 [ ] 1
3. As a result of meeting the learning objectives of this educational activity, will you be changing your practice performance in a manner that improves your patient care? Please explain. [ ] Yes [ ] No

_____

4. Did you perceive any evidence of bias for or against any commercial products? Please explain. [ ] Yes [ ] No

_____

5. How long did it take you to complete this CME/CE activity? ___ hour(s) ___ minutes
6. **Important for our planning:** Please state one or two topics that you would like to see addressed in future issues.

_____

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weeks, only patients who showed some response after one week were allowed to continue in the full trial—meaning that only 13 of the original 24 patients completed the trial.

After five weeks, patients taking adjunctive amphetamine showed a mean improvement in the Y-BOCS score of 48%, while patients on adjunctive caffeine improved by 55% (the difference was not statistically significant). Researchers were surprised to find that d-amphetamine worked no better than caffeine for OCD symptoms. They wrote that caffeine's good performance was probably not simply a placebo effect—instead, it may reflect d-amphetamine and caffeine's shared neurotransmitter effect of releasing dopamine in the brain (Koran LM et al., *J Clin Psychiatry* 2009;70(11):1530–1535).

TCPR's Take: This is a small study that did not include a true placebo arm, but these preliminary results are still intriguing. If both amphetamine and caffeine are actually effective for residual OCD symptoms (and we will need better studies to show this), then caffeine would probably be the preferable agent, given that it does not require a prescription and is unlikely to be abused. The 300 mg dose used in the study is the equivalent of almost two 8 oz cups of Starbucks coffee or 1.5 Vivarin caffeine pills (available over-the-counter at most drugstores for about $7 for 40).

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Next Month in *The Carlat Psychiatry Report*: Substance Abuse, including a review of Suboxone and an update on the use of drug testing to enhance treatment.

This Month's Focus:
The Diagnosis and Treatment of Dementia