The Carlat Report

On Psychiatric Treatment

AN UNBIASED MONTHLY COVERING ALL THINGS PSYCHIATRIC

VOLUME 1, NUMBER 10 WWW.THECARLATREPORT.COM OCTOBER 2003

Comparing Cholinesterase Inhibitors

If you were in *TCR*'s editorial offices, surrounded by boxes of articles about acetylcholinesterase inhibitors (AChEI's), you would quickly develop a sinking sensation. Not because the articles are so boring (though, in fact, they are); rather, because the pharmaceutical hype-sters are back on parade once again.

As with the SSRIs and the second generation antipsychotics, in which there are also several members of a class of meds, in the AChEI world there is intense jockeying for position, their are hired guns and pseudo-pharmacological advantages. *Caveat emptor*!

In this article, *TCR* compares the big three: Aricept, Reminyl, and Exelon. Sorry, Cognex (tacrine), but you don't make the cut. While you were the first to be approved in 1993, your bad habits of causing hepatotoxicity and bradycardia relegate you to a last-line bystander in this discussion.

Are the "pharmacological distinctions" relevant, or marketing ploys?

Let's begin with names. *TCR* has developed mnemonics for associating the brand with the generic names of these compounds. Aricept is donepezil (the first letters juxtaposed are "**AD**" for **A**lzheimer's **D**isease); Reminyl is galantamine (the drug helps you to "**Rem**ember a big **gala**"); Exelon is rivastigmine ("**Ex**(c)el on a **riv**er of memory"). Take them or leave them!

All these drugs have been subjected to rigorous placebo-controlled trials. Three different outcomes are often examined: cognitive functioning, ADLs, and "behavioral symptoms," a somewhat misleading term that includes depression and delusions as well as the truly behavioral problems like agitation and wandering.

Just to give you a sense of the methodology used, we'll look at a representative study, one published in 2000 in *Neurology* comparing Reminyl with placebo (1). For inclusion, patients had to meet standard criteria for Alzheimers

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Alzheimer's Dementia: A Primer

Plaques and Tangles, Amyloid deposits and Apo-E: Who can keep them straight? Unless you are a researcher, all you really need to know is how to diagnose dementia, and how to dose the acetylcholinesterase inhibitor *du jour*.

Nonetheless, being able to talk intelligently about current research is always a good thing for professionals, is certainly impressive to your patients, and may theoretically be entertaining for spouses during long road trips (but probably not).

Neuritic Plaques. On a slice of brain under the microscope, neuritic plaques look like ugly gobs of material crowding out neurons. But plaques begin their lives delicately, as a dance of scissor-like enzymes. At birth, all of our brains inherit a protein called **amyloid-precursor protein (APP)**. APP's function is not clear, but it is thought to do something useful in helping us to think our ways through life.

Eventually APP gets broken down by an enzyme called **alpha secretase**, with the residues dissolving harmlessly in the extracellular fluid, to be whisked away from the brain. But two evil enzymes, **beta and gamma secretase**, sometimes snip APP in the wrong places, leaving

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Next Month in *The Carlat Report*: Using antidepressants in children and adolescents: we sort through the latest confusing controversies.

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The Treatment of Dementia

Comparing Cholinesterase Inhibitors

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Dementia (AD), and their impairment could be no worse than "mild to moderate", that is, a Folstein Mini Mental State Exam (MMSE) score of 11-24; the average MMSE score in this study was 19. About 60% of patients were males, and the average age was about 75.

Patients were randomized to one of three treatment groups: placebo, moderate-dose Reminyl, or high-dose Reminyl. They were assessed periodically throughout the study with a well-loved measure of cognition in this research world: the ADAS-cog. It's confusingly scored, because a higher score means you're worse off, which is exactly the opposite of the MMSE.

The results were typical for what is reported for all AChEIs: The medication triggered a small cognitive boost within the first couple of months, which gradually petered away until cognitive functioning was at pre-drug baseline by the end of year one. By contrast, patients on placebo were already well below their cognitive baseline at the 6 month mark, with ADAS-cog scores a full 4 points above the Reminyl group, and 2 points above their baseline (yes, *above*--I told you the ADAS-cog was confusing!).

The problem was a high drop-out rate due to side effects (primarily G.I.), in the 20-30% range depending on the dose of reminyl, vs. only 8% drop-out on placebo. This type of data, not unique to Reminyl, is what drives the recommendations for a very gradual dose titration schedules for all AChEIs, and studies that have incorporated these schedules have reported much lower drop-out rates.

The bottom-line is that all AChEIs work for AD; in addition, each of the big three now sports convincing data for efficacy in *vascular dementia* as well.

What happens when patients stop taking their AChEIs? *Bad things.* A report in the *Archives of Neurology* compared two ultra-long term studies of Aricept (lasting about 3 years), both of which started as standard placebo-controlled trials. In one study, after 6 months of Aricept treatment, patients were switched to placebo for 6 weeks before being allowed to resume Aricept in an open label extension of the study. Cognitive scores plummeted in these patients, right down to the lowly level of those who had been on placebo since day one! And even when these patients were "rescued" with open-label Aricept, cognitive decline continued, with no real respite for the weary. This effect also occurred in the group that was more mercifully washed out for only 3 weeks, but it was not nearly as dramatic. The moral of this story? Once a patient is on an AChEI, don't let them interrupt it, come hell or high water.

Now, onto the pharmaceutical gamesmanship section of our article. Do the so-called pharmacological distinctions between the drugs hold up under *TCR's* magnifying glass?

1. Do nicotinic receptors matter? Janssen certainly hopes they do. Reminyl modulates presynaptic nicotinic receptors, which causes cholinergic neurons to churn out ever more acetylcholine (ACh), with the hoped for result that your patient's memory improves.

And there is actually some evidence in support of this point. A multi-center study conducted in the U.K. and funded by Janssen compared 94 AD patients on Reminyl with 88 patients on Aricept. (4) *After one year of treatment, Reminyl patients scored about 1.5 points higher on the MMSE than the Aricept patients.* The catch? This study was neither placebo-controlled nor double-blinded. Why is this important? Because participating doctors knew which drug they were prescribing, and may have raised patients' expectations with doctorly statements like: "Mr. Jones, we're going to be putting you on the newest and most powerful memory drug available--Reminyl!" Never underestimate the power of suggestion.

2. Does butyrylcholinesterase matter? BuCholE does exactly what ACholE does, namely, hydrolyzes and therefore inactivates acetylcholine. Exelon inhibits both BuChE and AChE, potentially making it more potent at revving up the cholinergic neurons. The problem is that most of the body's BuChE lives in the GI tract, and its inhibition probably explains why Exelon causes nausea in 47% of patients and frank vomiting in an astonishing *31%* (5). At this point, it appears that if BuCholE matters at all, it matters in a bad way for Novartis-worse tolerability than its competitors. ❖

***TCR*'s Cholinesterase Inhibitors Comparison Chart**

Brand name	Generic name	Dosing	Mechanism	Distinguishing Feature
Aricept	donepezil	5 mg QD X 4 weeks then 10 mg QD	Plain old AChE inhibitor	Easiest dosing
Reminyl	galantamine	4 mg BID X 4 weeks, then 8 mg BID; can go to 12 mg BID	AChE inhibitor *plus* nicotinic receptor modulation	Beat Aricept in one study
Exelon	rivastigmine	1.5 mg BID X 4 weeks, increase by 1.5 mg BID increments every 4 weeks up to 6 mg BID	AChE inhibtor *plus* BuChE inhibitor	Vomiting in 31% of patients

TCR VERDICT: *Aricept's Easiest; Reminyl Might be Better*

1. Raskind MA, Peskind ER, Wessel T. Galantamine in AD: A 6-month randomized, placebo-controlled trial with a 6-month extension. *Neurology* 2000;54:2261-2268.

2. Doody RS, Geldmacher DS, Gordon B. Open-label, multicenter, phase 3 extension study of the safety and efficacy of donepezil in patients with Alzheimers Disease. *Arch Neurol.* 2001;58:427-433

3. Wilkinson DG, Passmore AP, Bullock R. A Multinational, randomized, 12-week, comparative study of donepezil and rivastigmine in patients with mild to moderate Alzheimers Disease. *Int J Clin Pract* 2002; 56:441-446.

4. Wilcock G, Howe I, Coles H. A long-term comparison of galantamine and donepezil in the treatment of Alzheimer's Disease. *Drugs Aging* 2003; 20(10):777-789.

5. Package insert, rivastigmine.

Alzheimer's Dementia A Primer

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fragments that tend to clump together into **beta-amyloid deposits**, also known as "**A-beta**". A-beta then forms itself into insoluble beta-pleated sheets in between neurons. These sheets are not only neurotoxic, but also, being foreign bodies, attract white blood cells. Eventually, a whole morass of amyloid, dead neurons, and inflammatory tissue congeals to form neuritic plaques.

Neurofibrillary tangles. Meanwhile, via an apparently unrelated, but equally gory process, the scaffolding of our neurons is collapsing. **Tau** is a protein that supports the microtubules that keep cells in good shape. In old age, tau gets **hyperphosphorylated**, peals away from its microtubules, and forms **helical unions** with neighboring tau proteins. These helical filaments aggregate with others, eventually forming the infamous neurofibrillary tangles.

Acetylcholine. At this point, we are left with a picture of a pretty botched brain. Surveying the extent of the slaughter, one might assume that *any* neurotransmitters left would be zinging around in mazes and slamming into dead ends. So why the particular focus on acetylcholine?

Anyone who has taken a course in pharmacology recalls how much lecture time is devoted to **acetylcholine** (ACh). There are ACh receptors all over the body, explaining the multiple pesky actions of anticholinergic drugs (tachycardia, blurred vision, constipation, dry mouth, cognitive impairment). In the brain, most of the cholinergic neurons are concentrated in one particular area, toward the front, and close to the base. This area is called the **nucleus basalis of Meynert.** Long axons extend from the cholinergic cell bodies here to reach the hippocampus, the amygdala, and the cortex.

In Alzheimer's Disease (AD), plaques and tangles initially zero in on "Meynert," raining havoc preferentially on cholinergic neurons, which explains why drugs that increase ACh levels at this early stage are so effective. As AD progresses, degeneration spreads throughout the brain, eventually affecting the entire population of neurons and neurotransmitters.

Apo-E. Patients may ask you if they should be tested for "Apo-E" in order to determine their risk of getting AD. The scoop here is that apolipoprotein-E in itself is not at all bad, being a good all-around transport protein in the body. One of its functions is to bind with evil beta amyloid and clear it from the brain, thereby preventing the formation of plaques. However, a genetic variant of Apo-E, called E-4, is ineffective at binding to amyloid.

There are three different genetic versions (alleles) of the Apo-E gene: E2, E3, and E4. We inherit one allelle from each parent, so there are 6 different variations possible in our genetic make-up. If you are lucky enough not to have inherited E4 from either of your parents, you have only a 20% chance of getting AD by the time you're 80. If you are heterozygous for E4 (ie, you inherited E4 from only one parent), your risk goes up to 50%. If you are homozygous (E4 from both parents), you have, unfortunately, a 90% risk of AD by age 80. By the way, the Apo-E allele confers an even higher risk of AD if you are a woman.

So, should all your patients be offered Apo-E testing? A tricky issue. The test itself involves no more than a blood draw, and costs about $300 if paid privately, though some insurance companies cover it. However, most experts feel that the testing does more harm than good, because it causes such tremendous anxiety in patients who test positive, and there is little that can be offered to them in the way of preventing AD. ❖

TCR VERDICT: *Avoid Beta Amyloid; Don't Phosphorylate your Tau !*

Tales from THE HISTORY OF PSYCHIATRY: Call it "Alzheimer-Kraepelin's Disease"

Aloys Alzheimer was a German neurohistologist who was such a workaholic that he would examine brain tissue throughout the night, catching a few hours of sleep the next day before beginning all over again. His boss at the Heidelberg Clinic was none other than Emil Kraepelin (see *TCR* 1:9). In 1907 Alzheimer examined the brain of a 51 year-old woman who had arrived at the Clinic five years earlier with memory problems, and who had deteriorated rapidly since then. Under the microscope, Alzheimer discovered the now infamous plaques and tangles; however, it was actually Kraepelin who generated the concept that this represented a specific disease entity, and who gave it the nickname "Alzheimer's Disease." The name stuck, and catapulted an otherwise obscure histologist to a level of name recognition that will forever elude Kraepelin.

Q&A With the Expert

This Month's Expert:

Marc Agronin, M.D.
The Evaluation of Dementia

Director of Mental Health Services,
Miami Jewish Home & Hospital for the Aged
Assistant Professor of Psychiatry,
University of Miami School of Medicine

TCR: Dr. Agronin, as the "Director of Mental Health Services" at the Miami Jewish Home & Hospital for the Aged, what do you actually do?

Dr. Agronin: I serve as the full-time psychiatrist for a large long term care campus, with about 700 residents. Most of these are nursing home residents, but we also have almost 300 residents in the assisted and independent living towers. We have an outpatient clinic on the grounds, and in that clinic I work five days a week doing assessments of dementia and related psychiatric problems. I also supervise geriatric psychiatric fellows, medical students, and staff psychologists.

TCR: So you really do full-time geriatric psychiatry!

Dr. Agronin: Absolutely.

TCR: When a patient with suspected dementia comes into your clinic, how do you begin your evaluation?

Dr. Agronin: I begin with an open-ended question, like, "what brings you here?", and the manner in which they answer this question often provides important clues. Are they able to respond coherently, are they able to provide both recent and remote history, is their version of events consistent with the informant's?

TCR: Do you often have a pretty good sense of whether or not a patient has dementia within the first 5 minutes?

Dr. Agronin: If the question is, "Is there dementia, yes or no?", then yes I do. But getting at the specific type of dementia is more difficult, although 7 times out of 10 if you say "Alzheimer's Disease" you're going to be correct.

TCR: My sense is that in the community, many non-geriatric psychiatrists may be tempted to cut corners diagnostically, and say, "Well, this patient is demented, and I'm going to put him or her on cholinesterase inhibitors regardless of the type...."

Dr. Agronin: Well, it's certainly true that ultimately, most roads will lead to the use of cholinesterase inhibitors, but the reason it's important to carefully ascertain the baseline and the course of the dementia is that it can help you find reversible causes. Probably 10-15% of cases of dementia have reversible factors, usually either a medical disorder or a medication related factor. Also, depression in particular can be associated with cognitive impairment.

TCR: When you do your work-up to rule out reversible causes, what are some of the things that you always do?

Dr. Agronin: First, I review the meds that they're on, and I ask specifically about antihistamines, narcotics, steroids, and tricyclic antidepressants (which are used more for chronic pain than for depression these days.) Recent research has shown that many medications have unexpected anticholinergic properties, including digoxin, furosemide, theophylline, warfarin, and isordil, and when these are used in combination you begin to have an impact on cognition. A mild anticholinergic delirium can be deceptive, since it may wax and wane over the course of months, and may be misdiagnosed as an insidious progressive dementia.

The 'Mini-Cog'

"I find the Mini-Cog to be one of the most efficient ways of doing a dementia screening, because it's shorter than the MMSE and it gives you the same information."

TCR: Any other important medical factors?

Dr. Agronin: Risk of stroke is a very major one. Anything you can do to decrease the risk of stroke probably lowers the risk of Alzheimer's Disease. In addition, I always get thyroid function tests to rule out hypothyroidism, calcium levels to rule out hypercalcemia and I always order a head CT-it's quick, economical, and it will rule out strokes or lesions. I'll often also often order an RPR (to rule out neurosyphillis), folate, B12, and in some settings and HIV test.

TCR: How do you usually assess for memory impairment?

Dr. Agronin: I don't jump right into structured questions. I like to start with an easy-going conversation, as if I'm interviewing them for an article about their life. So I ask them about what they enjoy doing, about their relationships with family members, about where they live, what type of work they've done, and about their hobbies, both currently and in the past.

TCR: So this is kind of like a fireside chat!

Dr. Agronin: Yes, and this is one reason I love geriatric psychiatry so much, because you get the most amazing historical accounts,

Q & A With the Expert

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and this helps you humanize the patient behind the dementia, which is often critical to diagnosis and treatment.

TCR: And what's going on in your mind as you are listening to their stories?

Dr. Agronin: I note whether the detail is logically put together, and whether there are any obvious gaps. If I know about the reported historical events, I might question them in particular about those; for instance, I have a special interest in World War II history and I can often assess the accuracy of their memory by asking about their military history in some detail.

TCR: So here, you're assessing memory loss, which is the cardinal feature of dementia.

Dr. Agronin: Exactly. I'm also assessing how well they use language to express themselves. You can pick up on varying degrees of aphasia in simple conversation. You can also pick up on agnosia (impairment in recognition of familiar people or objects) as they tell their story. Once I have built up some rapport, I eventally get into a more structured mental status evaluation.

TCR: How do you generally approach that?

Dr. Agronin: For me, the two most helpful tasks are the three-item recall and the Clock-Drawing Task (CDT). Some researchers have put these two tasks together and have called it the "Mini-Cog"(1). I find it to be one of the most efficient ways of doing a dementia screening, because it's shorter than the Folstein Mini Mental State Exam (MMSE) and it gives you the same information.

TCR: How do you actually do the three-item recall?

Dr. Agronin: I'll usually introduce it by saying, "I'd like to do a brief test of your memory. I'm going to say three words to you, and I want you to repeat them back to me and memorize them." I'm in the habit of using the words "apple, penny, and table," although it doesn't matter what three words you use as long as they don't rhyme or alliterate. Then I'll have them do another task (such as the CDT), and 3 to 5 minutes later I'll ask them to repeat the words.

TCR: How do you interpret the results?

Dr. Agronin: If they get all three words right, then the chances of dementia fall substantially; if they can't remember any of them, dementia is very likely. If they remember one or two, the CDT provides an enormous amount of additional information.

TCR: And how do you conduct this test?

Dr. Agronin: I'll hand them a piece of paper and a pen and ask them to draw a clock that reads "11:10."

TCR: Why do you find it so useful?

Dr. Agronin: Because it measures literally every component of dementia. You measure memory because they have to remember the instructions. You identify apraxia by assessing their ability to make a drawing of the clock and to lay out the numbers correctly. You assess agnosia by noting whether they even recognize what a clock looks like. You measure mathematical ability by seeing whether they can correctly translate the "10" into the "2" on the clock face. It's also an excellent test for executive functioning-their ability to plan and sequence the task. And the MMSE is notorious for not being a good measure of executive functioning.

TCR: How do you proceed with the rest of your evaluation?

Dr. Agronin: I look for all the other elements of the mental status examiniation. I look for apathy, psychosis, depression. It's important to have the informant weigh in as well, because some people have their social graces preserved and it's easy for them to cover up a problem. I ask the informant how the patient has been functioning. How well can they manage money, medications, and daily appointments? I ask about day-to-day household things. Can they keep themselves clean, and can they keep the house clean? How are they doing with driving?

TCR: How do you break the news of dementia to patients and family?

Dr. Agronin: I focus more on the issue of memory, and I typically will not use the words "dementia" or "Alzheimer's Disease" because usually at the first evaluation I don't know for certain anyway and I don't want to use any buzzwords that will be upsetting.

TCR: So at what point are you pretty certain about the diagnosis of dementia?

Dr. Agronin: I usually have a good hunch at the end of the first interview but I often hold off until I have the results of neuropsychological testing.

TCR: Do you always request neuropsychological testing?

Dr. Agronin: In 90% of cases, I do.

TCR: How do you find it useful?

Dr. Agronin: The tests I use during my evaluation are merely screening tests. They tell me "probably dementia," or "probably not dementia." They don't tell me the type of impairment. Neuropsych testing will quantify and qualify the area of impairment, and may help me distinguish AD from another type of dementia, such as a vascular dementia or a Lewy Body Dementia.

1. Borson S, Scanlan J, Brush M et al. The Mini-Cog: A cognitive 'vital signs' measure for dementia screening in the multilingual elderly. *Int J Geriatr Psychiatry* 2000;15:1021-1027.

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Preventing Dementia: What Works

We'd all like to escape dementia in our old age. Over the past decade, numerous large scale epidemiological studies have been published singing the praises of a variety of agents that might prevent or delay dementia. Of course, ever since the recent estrogen debacle, in which early promising observational findings were completely overturned by a well-designed clinical trial, we are all a little reluctant to believe what the epidemiologists are telling us. Nonetheless, we have to work with the data that we have, and here it is.

The Memantine Story

No, contrary to all appearances, memantine is *not* yet FDA approved for dementia. A spate of Forest-funded journal supplements and CME-Inc courses are apparently aimed at whetting our appetites, but they are about 6 months early. Memantine is an NMDA antagonist, and tries to prevent too much glutamate from pounding neurons already surrounded by beta-amyloid glue. The studies so far show modest efficacy, no better than the AchEIs, (and no better for severe dementia than AChEIs.) One study finds it to be an effective adjunct to Aricept, and this plus its good side effect profile will likely make it popular.

NSAIDs. Since much of the cell destruction in AD may be related to inflammatory processes, an anti-inflammatory may be helpful in slowing the progression. The first indication that this might be true came from the curious finding that people with rheumatoid arthritis tended not to become demented. Medication-wise, what separates these patients from everyone else? The use of non-steroidal antiinflammatories (NSAIDs).

Since then, large observational studies have been conducted. The usual method is to identify a large number people in the community, to ascertain how many of these people took NSAIDs and for how long, and then to find out which patients developed AD, either by looking at their charts or interviewing them. You don't have to be a research whiz to see that this method is vulnerable to serious problems. For example, these studies may not have ascertained exactly which NSAIDs were taken, what the doses were, or exactly how long they were taken, all of which are good things to know when you are advising your patients.

Nonetheless, a recent large study from the Netherlands (1) was better designed than most, and has convinced many in the research world that NSAIDs are probably protective against AD, but only if they are taken for at least 2 years straight. Patients who were on NSAIDs for at least two years were only 20% as likely to develop AD as those who were NSAID free.

Vitamin E. Don't tell me you didn't start prescribing megadoses of vitamin E to your elderly patients after the famous *NEJM* article of 1997 (2). Yes, I'm talking to you!

We all did, because that data appeared so compelling, and vitamin E appears so harmless. To refresh your memory, that was the study in which 341 moderately demented patients with AD were randomly assigned to 2000 International Units (IUs) of vitamin E, 10 mg/day of selegiline, the combination of the two, or placebo. Compared to placebo, vitamin E delayed a bad functional outcome by 230 days-not bad for something you can pick up at your neighborhood General Nutrition Center. While a few other similar studies have modestly supported a protective effect of vitamin E, a recent fancy meta-analysis of a range of antioxidants (including vitamin E) found that they were of absolutely no benefit in the prevention of a different entity-cardiovascular disease (3). And while dementia is something entirely different, this finding has deflated everyone's enthusiasm for prescribing vitamins for the prevention of major disorders.

Ginkgo Biloba. Like vitamin E, 1997 was a golden year for ginkgo biloba, when a *JAMA* study showed that 26 weeks of ginkgo biloba boosted cognitive functioning in patients with AD more than placebo (4). Since then, studies have been quite mixed, however. An effort to replicate these findings, using a basically identical study design in 2000, failed miserably (5). And randomized controlled studies of ginkgo used by cognitively normal people have been inconsistent.

At this point, the true benefit of ginkgo is too close to call. But it's pretty darned safe, and many people swear that they think more sharply when they are on it. ❖

TCR VERDICT: *Preventing Dementia: Lower Your Expectations*

1. In't Veld BA, Ruitenberg A, Hofman A, et al. Nonsteroidal antiinflammatory drugs and the risk of Alzheimer's disease. *N Engl J Med* 2001; 345:1515-21.
2. Sano M, Ernesto C, Thomas RG, et al. A controlled trial of selegiline, alpha-tocopherol, or both as treatment for Alzheimers Disease. *N Engl J Med* 1997;336:1216-1222.
3. Vivekananthan DP et al. Use of antioxidant vitamins for the prevention of cardiovascular disease: Meta-ananlysis of randomised trials. *Lancet* 2003;361:2017-23
4. Labars PL, et al. A placebo-controlled, double-blind, randomized trial fo an extract of ginkgo. *JAMA* 1997;278:1327-1332.
5. van Dongen MCJM et al.The efficacy of ginkgo for elderly people with dementia and age-associated memory impairment: New results of a randomized clinical trial. *J Am Geriatr Soc* 2000;48:1183-1194

ANECDOTES FROM THE FIELD: Beware Benadryl!

Dr. Renee Snow completed a geriatric psychiatry fellowship at Mclean Hospital and is now in private practice in North Andover, MA.

"One important question I ask in evaluating elderly patients is 'what over-the-counter medications have you been taking?' A lot of older folks are taking Tylenol PM for sleep, which has Benadryl in it, or often they are taking straight Benadryl. These preparations often impair cognition, and I'll usually switch them to trazodone 12.5-25 mg QHS for sleep. Another very common anticholinergic is meclizine, and many people won't report taking it unless you ask about it specifically."

CME Post-Test

To earn CME credit, you must be a subscriber of *The Carlat Report* and complete the following quiz, answering at least 5 of the 6 questions correctly. Select the best answer, circle the letter corresponding to your choice, and mail this page to CME Coordinator, The Carlat Report, P.O. Box 626, Newburyport, MA 01950. You may also fax the answer sheet to the CME Coordinator at (978) 499-1892. Anna Jaques Hospital (AJH) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing education for physicians. AJH designates this educational activity for a **maximum of 1 hour credit** toward the AMA's Physician Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

1. The cholinesterase inhibitor Aricept:
- a. Is noted for causing the most GI distress
- b. Is the only AChE inhibitor that can be dosed once a day
- c. Causes a sustained rise in MMSE scores over more than one year
- d. Is also an NMDA receptor antagonist

2. A true statement about Reminyl is:
- a. The starting dose is 1.5 mg BID
- b. It is the only AChE inhibitor to show efficacy in vascular dementia
- c. One study showed better efficacy than Aricept, but the methodology was questionable
- d. It inhibits BuChE more strongly than Exelon

3. The enzyme alpha secretase leads to plaque formation.
- a. True b. False

4. Non-steroidal antiinflammatories (NSAIDs):
- a. May help to prevent dementia, but only if used for two years or more
- b. Cannot be used long-term because of GI side effects
- c. Have about the same effects on cognition as memantine
- d. Have been shown to be superior to vitamin E for dementia

5. The Mini-Cog:
- a. Is the primary assessment tool used in dementia research
- b. Is identical to the Folstein Mini Mental State Exam
- c. Is a single question screen for dementia
- d. Combines the three-item recall and the clock-drawing task

6. Dr. Agronin's suggestions for the dementia work-up include:
- a. A careful assessment of concurrent medications for anticholinergic properties
- b. Neuropsychological testing *before* the initial interview
- c. PET scanning for most patients
- d. Avoiding lab tests because of the risk of false-positives

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This Month's Focus:
The Treatment of Dementia