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Editor-in-Chief

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IN THIS ISSUE

Focus of the Month:
Treatment of Dementia

Learning objectives for this issue:
1. Describe current pharmacological treatment of dementia. **2.** Explain some of the different types of dementia. **3.** Diagnose and treat psychiatric illnesses in the elderly. **4.** Understand some of the current findings in the literature regarding psychiatric treatment.

Current Pharmacological Treatment of Dementia

Cary S. Gunther, PhD, MD
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Dr. Gunther has disclosed that she has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

Patients with dementia and their families may express frustration about the limited number of options for improving cognitive symptoms, but they are not without choices. Here we will review a number of pharmacological treatment options for Alzheimer's disease (AD) and other major types of dementia.

Cholinesterase Inhibitors

The use of cholinesterase inhibitors in treatment of dementia is based on

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In Summary

- Treatments for dementia include the cholinesterase inhibitors Aricept, Exelon, Razadyne, and tacrine and the NMDA glutamate receptor antagonist Namenda.
- CIs yield modest cognitive benefits, as does Namenda, alone or as an adjunct to CIs.
- Depression is best treated with SSRIs.
- Parkinsonian symptoms and insomnia are treatable with medication, but beware of side effects in the elderly.

Q&A With the Expert

Psychiatric Illness in the Elderly

Dan G. Blazer, MD, PhD

Vice Chair, Department of Psychiatry and Behavioral Sciences
Vice Chair, Academic Development
Duke University

Dr. Blazer has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

TCPR: Apart from the obvious problems like memory disorders and dementia, what should we know about psychiatric issues in the elderly?

Dr. Blazer: One thing to begin with is to recognize that in general surveys of happiness, contentment, and well-being, older persons for the most part score *higher* than people in midlife and certainly in earlier young adulthood. So most conditions, other than the neurocognitive disorders, are actually less frequent in the elderly. You may see what people call "burnout" as individuals get into late life, in which depressive disorders, substance use disorders, manic disorders, and others, decline over time. But it doesn't mean that they are less important. For example, the suicide rate was higher among older persons than in any other age group throughout the 20th century.

TCPR: Are there special considerations when evaluating older adults with psychiatric disorders?

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Current Pharmacological Treatment of Dementia

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the cholinergic hypothesis, which suggests that deficits in cholinergic neurotransmission (caused by death and dysfunction of neurons that use acetylcholine) are responsible for much of the cognitive decline in dementia, particularly in AD (Bartus D et al, *Science* 1982;217(4558): 408–414). Cholinesterase inhibitors block the enzyme that breaks down acetylcholine in synapses, yielding higher concentrations of this neurotransmitter for longer periods of time. Four medications in this class are approved for use in dementia treatment: tacrine (Cognex), donepezil (Aricept), rivastigmine (Exelon), and galantamine (Razadyne). Tacrine is rarely, if at all, used at present because of dose-related hepatotoxicity that has not been seen with the other agents.

Donepezil is available in 5 mg and 10 mg tablets and is approved for all stages of AD. The 10 mg dose has been established as more effective than the 5 mg dose.

The lower dose pill is ideally used for a month before increasing to 10 mg so as to minimize side effects during initiation of therapy. A 23 mg dose is also available for patients with moderate to severe AD who have been maintained on 10 mg.

Rivastigmine comes in oral tablets or as a daily transdermal patch. The oral formulation is associated with greater gastrointestinal upset so is less commonly used. Patch doses are 4.6 mg, 9.2 mg, and 13.3 mg. The 4.6 mg patch is intended as a titration, rather than maintenance, dose, with increase to 9.2 mg after four weeks and possible further increase after an additional four weeks. Rivastigmine undergoes largely extrahepatic metabolism and so has relatively few pharmacokinetic interactions with other meds. It is also marketed for dementia secondary to Parkinson's disease (PD).

Galantamine is available as 8 mg and 16 mg tablets, with 16 mg established as an effective dose. This medication is also available in sustained-release formulation, up to 24 mg per day. Doses are increased at four week intervals.

Side effects of cholinesterase inhibitors can include gastrointestinal disturbances (nausea, vomiting, diarrhea), muscle cramps, vivid dreams or insomnia, and rhinorrhea. GI upset is significantly more prevalent at the highest doses and it is not uncommon for patients to need to return to a lower dose when this occurs. Rarely, these medications can produce bradycardia; however, it can be symptomatic when present. Be careful of these drugs in patients with supraventricular cardiac conduction defects (reviewed in Schneider LS, *Continuum* 2013;19(2):339–357).

How Well do They Work?

Donepezil and galantamine, in particular, may provide benefit in treatment of vascular cognitive impairment in addition to AD, although no member of the class has an FDA indication for treatment of vascular dementia. Nonetheless, cholinesterase inhibitors may yield behavioral benefits and improved activities of daily living (ADLs) in this population (reviewed in Gorelick PB and Nyenhuis D, *Continuum* 2013;19(2):425–437).

Cholinesterase inhibitors as a class yield modest cognitive benefits in dementia patients that have largely been demonstrated over six months to one year (reviewed in Birks J, *Cochrane Database Syst Rev* 2006;1:CD005593).

You may wish to explain to patients and families that these medications are intended to stabilize current function and defray cognitive losses and that actual reversal of deficits is unlikely. There is no reason to combine medications from this class, and the choice among members of the class may be based on side effects profiles, pill burden or formulary constraints. Head to head comparisons among cholinesterase inhibitors have not been done.

Memantine

Memantine (Namenda) acts as an antagonist at NMDA glutamate receptors and is thought to work by preventing glutamate-induced neurotoxicity. This medication is FDA approved for treatment of moderate to severe AD. Its efficacy has been demonstrated in patients already taking cholinesterase inhibitors, and this is how it is primarily intended to be used. However, memantine can be given to patients *not* taking cholinesterase inhibitors, for example, if tolerability of cholinesterase inhibitors is poor.

The effects of memantine were demonstrated using tests of severe impairment and measurements of ADLs, rather than cognitive tests that highlight milder degrees of cognitive impairment (reviewed in Schneider ibid).

Dosing of memantine begins with 5 mg daily and reaches 10 mg twice daily over the course of a month. A 28 mg sustained-release dose has been FDA approved but not yet marketed. Infrequent side effects include headache, somnolence, and dizziness. Significant sleepiness at the higher end of dose titration may necessitate discontinuation or decrease.

As with cholinesterase inhibitors,

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Current Pharmacological Treatment of Dementia
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the cognitive benefits of memantine are modest and seen over six to 12 months. Perhaps the goal of treatment with this medication is best explained to patients as a delay in cognitive decline of up to a year. Memantine is not well studied in vascular cognitive impairment but some studies have suggested benefit (reviewed in Gorelick PB and Nyenhuis D, *Continuum* 2013;19(2):425–437).

Treatment of Sleep Disturbance

Insomnia and disrupted sleep are common findings in all types of dementia. Treatment of these complaints is complicated by the greater sensitivity of elderly and cognitively impaired individuals to excessive sedation, as well as disinhibition and side effects that can accompany commonly used GABAnergic agents such as benzodiazepines and zolpidem (Ambien).

Options include melatonin, which has been shown to be effective in dementia (Mayer G et al, *Sleep Med Rev* 2011;15(6):369–378), and trazodone (Oleptro, Desyrel). As an alpha-adrenergic antagonist, trazodone may cause orthostasis at higher doses, but it may be particularly helpful for agitated and disturbed behavior in frontotemporal dementias (FTD) (reviewed in Mendez MF, *Front Neurol Neurosci* 2009;24:168–178).

Depression in Dementia

Depressive symptoms are common in vascular dementia and AD as well as in PD, which can commonly produce a dementia syndrome. It may be difficult to establish a firm diagnosis of depression, because symptoms such as poor concentration and loss of interest in activities can often be attributed directly to dementia. Moreover, in a geriatric population, somatic and neurovegetative complaints may predominate over subjective complaints of low mood.

Nonetheless, depressive symptoms warrant attention. SSRIs are generally first line because of their safety profile. Avoid MAOIs, tricyclics, and other agents with significant anticholinergic burden as these may increase confusion.

It is important to think about distinguishing depression from apathy and abulia that are direct products of neurodegenerative diseases and are often more distressing to caregivers than to patients. For this purpose, consider antidepressants with dopaminergic properties, such as sertraline (Zoloft) and bupropion (Wellbutrin), or judicious use of stimulants (Burke A et al, *Continuum* 2013;19(2):382–396).

Parkinsonian Symptoms

Parkinsonian symptoms may be seen in later stages of any dementia. They are often present in frontotemporal degeneration and, of course, in the "Parkinson's-plus" syndromes corticobasal degeneration (CBD), progressive supranuclear palsy (PSP), and dementia with Lewy bodies (DLB). These Parkinsonian symptoms are generally less responsive to medications than are the motor symptoms of idiopathic PD. Options include levodopa/carbidopa (Sinemet) and dopamine agonists.

Beware of side effects such as compulsive behaviors and hallucinations when using dopamine agonists. When Parkinsonian syndromes require treatment, you will want to seriously consider partnering with a neurologist experienced in dosing these medications (Seltman RE and Matthews BR, *CNS Drugs* 2012;26(10):841–870).

Agitation and Psychosis

No agents have been approved for the specific treatment of agitation in dementia patients. Nevertheless, behavioral disturbances are common and warrant treatment for the comfort or safety of the patient as well as the maintenance of a safe environment for caregivers. The first line is to use agents already established for use in AD: cholinesterase inhibitors and memantine, which may ameliorate aggression and psychotic behavior even when cognitive benefits are not noticeable (Trihn, NH et al, *JAMA* 2003;289(2):210–216; Cummings, JL et al, *Neurology* 2006;67(1):57-63).

Cholinesterase inhibitors appear to show behavioral benefits in dementia with Lewy bodies as well (reviewed in Wild, R, et al, *Cochrane Database Syst Rev* 2003;3:CD003672). SSRIs are sometimes used in FTD to decrease disinhibition and compulsive behaviors (reviewed in Mendez, MF, *Front Neurol Neurosci* 2009;24:168–178). Use of mood stabilizers or antiepileptics has limited evidence support and often generates more side effects.

In the acute setting, antipsychotics may be necessary, though their use is problematic as well. First and second generation antipsychotics alike carry the infamous "black box warning" for risk of sudden cardiac death in the elderly, and may cause sedation, orthostasis, and falls. These agents can be difficult to discontinue but attempts should be made to do so anyway. They are not a substitute for behavioral interventions (see Burke et al, op.cit.).

Elderly patients are more susceptible than the general population to parkinsonian effects of antipsychotics, and these agents must be used sparingly, and not at all if DLB is suspected. Quetiapine (Seroquel) is often the agent of choice and doses as low as 12.5 mg may be appropriate (Ballard C et al, *Lancet* 1998;351(1908):1032–1033).

The Future of Dementia Treatment

Although no new medications for treatment of dementia have come to market in several years, this is certainly a field of active research. Current avenues of investigation include immunization-based approaches (passive immunization as well as attempts at vaccine development); compounds that would inhibit the aggregation or activity of the Tau protein, which plays a role in AD as well as FTD; modulation of the synthesis or processing of amyloid; and treatments aimed at addressing the brain insulin resistance that has been observed in AD.

Although trials of some agents have been halted because of weak results, there are still additional compounds under study, and some existing approaches are being modified to see if specific subgroups of dementia patients may respond.

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Expert Interview
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Dr. Blazer: Yes. Psychiatric disorders in late life occur in individuals who are generally more vulnerable, either in terms of their cognitive capacity or their physical health. So the consequences of a psychiatric disorder in late life can be very significant. We must be very careful not to discount symptoms: when an older person begins to complain of sleep or appetite problems or begins to look depressed, that is something that really deserves attention.

TCPR: So what symptoms or psychiatric complaints should we be looking for to determine which patients need more aggressive psychiatric help?

Dr. Blazer: A good marker for understanding older persons is not the diagnosis of a specific illness, but rather the function of the individual. How much is the person getting up and walking around? Can the person take care of his or her daily needs, such as keeping up with the checkbook, buying groceries, or driving? Really looking at the spectrum of what the older person is capable of doing will tell us more than simply focusing on a diagnosis. Furthermore, it is important not to separate the psychiatric help from treatment for the physical disorders, because they are comingled. For example, say an elderly man is tired, he has lethargy, is down, and is having difficulty sleeping. He may very well be suffering from depression, but that depression also may be superimposed on chronic obstructive pulmonary disease. Finally, a very important part of geriatric medicine is the understanding of frailty and failure to thrive. Older people can sometimes pass a threshold beyond which they will not eat, they seem to be depressed, they are very lethargic, and if you don't turn that around, the result is continuing decline and possibly death. Depression and cognitive difficulties can certainly be a part of that; but importantly, we can't say we are going to deal with these symptoms and not be concerned about the others.

A good marker for understanding older persons is not the diagnosis of a specific illness, but rather the function of the individual.

Dan G. Blazer, MD, PhD

TCPR: Tell us about mood disorders in the geriatric population.

Dr. Blazer: One thing to keep in mind is that older persons often will not use the term "depressed," but the good news is that they are usually very cooperative and willing to work with the psychiatrist once they get to you. The most significant symptom is anhedonia. A typical thing a depressed older person will say is, "I love my grandkids. I used to really enjoy them coming over to the house. I still care a lot about them, but I just can't get excited to know that they are coming, and sometimes am glad that they are ready to go when they go," Or they will say, "I eat because I *need* to eat." So their interest in food will decline and they might report weight loss. Sleep problems are also very common. Older persons, in general, have sleep problems anyway, but what we see with depressed older persons is that they will awaken frequently, and they realize that they have awakened frequently.

TCPR: What are some of the methods and principles we should keep in mind when treating this population?

Dr. Blazer: There is a fairly substantial literature supporting the combination of one of the more "educationally-oriented" or cognitively-oriented psychotherapies along with medication use as the best way to treat these individuals, both in relieving their initial symptoms and in preventing the recurrence of symptoms. With medications, you want to start low and go slow in your dosage. This is a reasonable rule of thumb for someone who is maybe 75 years of age and older. For example, if you are using a drug like paroxetine where your usual dosage might be 20 mg, you might want to start with 5 mg, try that for a while and then work up gradually to your target dose. Generally they will need and often will tolerate a regular dose of the medication, but you don't want to start them on that initially because of the potential for side effects, which will undermine your ability to treat them. All of the medications that we use earlier in life can be effective in later life.

TCPR: So any antidepressant that is effective for depression in the young is good for the elderly as well?

Dr. Blazer: Yes. For people who are very old, and have a lot of lethargy and apathy, sometimes a very low dose of methylphenidate can be effective, too. I mean about 5 mg once or twice a day, and never after 2 o'clock in the afternoon. The best treatment is a combination of medications and behaviorally-oriented, educational psychotherapy.

TCPR: Which types of therapy work best?

Dr. Blazer: Interpersonal therapy and cognitive behavioral therapies are effective sometimes on their own in treating older persons. If you have an older person who really cannot take a medication, perhaps for medical reasons or for significant side effects, then certainly it is worth a trial of cognitive behavioral therapy. If the depression is moderate to severe, and if it does not respond to medications, then I recommend thinking about brain stimulation techniques. Of course ECT has been around for the longest and it can be very effective in treating older persons. And the memory problems that were the bane of ECT for many years are less worrisome now when nondominant treatments are used and when you really monitor these individuals very carefully. There are some other brain stimulation techniques that have been used on depression in the elderly: transmagnetic stimulation is one example.

TCPR: What can you say about the use of benzodiazepines, anticholinergics, and antipsychotics, given the potential risks of these drugs in the geriatric population?

Dr. Blazer: Let's take the benzodiazepines first: older persons are more likely to experience adverse effects with benzodiazepines than are people who are younger, all other things being equal. On the other hand, older persons, in my view, are less likely to become addicted or abuse them. So benzodiazepines *can* be used judiciously. I would recommend the short-acting benzodiazepines like lorazepam, for example, or alprazolam, as opposed to some of the longer acting ones. There is no reason that the benzodiazepines are absolutely contraindicated in older persons, but you should be careful of potential for falls in patients taking these.

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Types of Dementia			
Type of Dementia	**History**	**Signs and Symptoms**	**Pathology/Imaging**
Alzheimer's Disease (50–80% of all dementia cases)	Gradual, progressive onset	• Memory loss, especially for names and recent events • Language deficits • Rapid forgetting • Impaired visuospatial skills • Normal gait and neuro exam early • Later affective disturbances; behavioral symptoms such as aggression	• Generalized atrophy (esp. medial temporal) • Beta amyloid plaques • Neurofibrillary tangles
Vascular (20–30%)	Abrupt or gradual onset	• Focal neurological signs • Signs of vascular disease	• Strokes • Lacunar infarcts • White matter lesions • Vulnerable to cerebrovascular events
Lewy Body (10–25%)	Insidious onset, progressive with fluctuations	• Fluctuating cognition • Visual hallucinations • Neuroleptic sensitivity • Shuffling gait • Increased tone • Tremors • Falls	• Generalized atrophy • Lewy bodies in cortex and midbrain
Frontotemporal (10–15%)	Insidious onset, typically in 50s–60s; rapid progression	• Disinhibition • Socially inappropriate behavior • Poor judgment • Apathy, decreased motivation • Poor executive function	• Frontal and temporal atrophy • Pick cells and pick bodies in cortex

Expert Interview

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TCPR: And the anticholinergics?

Dr. Blazer: You generally want to avoid anticholinergics, especially in older persons who have memory difficulties. At one time a low dose of amitriptyline was used to help older people sleep. A better option now is a very low dose of trazodone, as low as 25 mg, which might give you the same effect without the problem of the anticholinergic effects.

TCPR: And finally, the antipsychotics?

Dr. Blazer: Physicians have hotly debated the topic in geriatric psychiatry, specifically the use of antipsychotics in nursing home populations. On the one hand, there has been a recent drive to reduce the regularity of nursing home patients taking these. On the other hand, there are older persons who are very agitated who cannot be managed pharmacologically without an antipsychotic medication. In this case, the new generation drugs are generally preferred, as patients can tolerate using those drugs for a long time, and sometimes you can rotate on and off.

TCPR: Earlier you mentioned burnout of certain conditions. Is mania one of these? Does it wane with age?

Dr. Blazer: Mania is somewhat less prevalent in old age, and even individuals who have had significant and frequent episodes of mania when they were younger might have less frequent or no manic episodes at all when they get into late life. What is important to recognize, though, is that mania can present in different ways in older persons. What we tend to see is more agitation and irritability than what we typically think of as mania, where the person is joyous, euphoric, and full of energy. Sometimes mania can even be misinterpreted as depression. In such cases, as in younger patients, the person may be put on an antidepressant that might exacerbate the mania. So I think recognizing how mania presents is very important. Mania certainly can present with psychotic episodes; in fact, it probably is more likely to present with psychotic symptoms later in life than it is earlier in life.

TCPR: What ways can people age happily?

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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 educational activity.

SUICIDE

A Blood Test for Suicide?

Prediction of suicidal behavior has long been considered more of an art than a science, although the use of clinical and demographic features can help improve risk assessment (see, for instance, *TCPR,* June 2012). An accurate biological test or "biomarker" for suicidality would be valuable, and a recent study takes us one step closer to that goal.

In preliminary work, researchers retrospectively evaluated blood samples from 75 patients with bipolar disorder, collected at multiple office visits, and found 41 genes that were expressed differentially (ie, to a significantly greater or lesser degree) when the patients expressed suicidal ideation. Of these 41, 13 were also differentially expressed (12 higher, one lower) in nine randomly-selected men from the local coroner's office who had committed suicide. Six of these remained significantly elevated after rigorous statistical testing.

Separately, the same researchers studied gene expression in 88 men with bipolar disorder (n=42) or psychosis (n=46), and found that four out of these six genes were more highly expressed in patients who had ever been hospitalized for suicidality. The predictive power of these tests was enhanced when combined with simple questions regarding subjective measures of mood, anxiety, and psychosis.

The most predictive biomarker was a gene called *SAT1,* while others included *PTEN, MARCKS,* and *MAP3K3*. The *SAT1* protein is an enzyme involved in the breakdown of polyamines, and overexpression of *SAT1* in mice causes infertility and weight loss, among other symptoms. A gene called *CD24* was underexpressed in suicidal patients, and the *CD24* protein is involved in preventing apoptosis, or programmed cell death. Thus, some of the genes identified in the study seem to function in processes that may relate to cell survival.

A key strength of the study was its use of microarray technology to screen for thousands of genes at a time. Another, as noted above, was that it relied on biological measures, not interview questions, which can be unreliable. Weaknesses include the fact that subjects were all male Caucasians with bipolar or psychotic disorders (not unipolar depression). Also, samples were taken from peripheral blood, not the "target organ," the brain. While this permitted easy collection of samples, the accuracy of such measures may be questioned (Le-Niculescu H et al, *Molecular Psychiatry* 2013, online ahead of print).

TCPR'S TAKE: To predict suicide on the basis of a blood test seems paradoxical, since suicide is an inherently personal decision: the ultimate in "free will," so to speak. The current research suggests that this may not entirely be the case. But before we bring this "bench" research to the bedside of patient care, we should wait for replication of these results (including in other patient populations), and explore whether interventions to normalize or reverse these biomarkers have a protective effect.

News of Note

ANTIPSYCHOTICS

APA Warns Against Common Uses of Antipsychotics

In September, the American Psychiatric Association (APA) released a list of common, but potentially dangerous and inappropriate, uses for antipsychotics. The APA's list includes the following recommendations:

- Don't prescribe any antipsychotics without an appropriate initial evaluation and ongoing monitoring
- Don't routinely prescribe two or more antipsychotic medications together
- Don't prescribe antipsychotics as first-line treatment for behavioral and psychological symptoms of dementia
- Don't routinely prescribe antipsychotics as first-line treatment of insomnia in adults
- Don't routinely prescribe antipsychotics medications as first-line treatment in children and adolescents for anything except psychotic disorders

The list was released as a part of the *"Choosing Wisely"* initiative, a program developed by the American Board of Internal Medicine (ABIM) Foundation to encourage physicians and their patients to discuss medical tests and procedures that may be unnecessary or harmful. *Choosing Wisely* currently lists more than 250 tests or procedures that may be harmful to patients. More than 80 specialty societies and groups have signed on to the program.

More information the APA's recommendations can be found at www.psychiatry.org/choosingwisely

NEW DRUG APPROVAL

Vortioxetine (Brintellix) approved for MDD

The FDA has approved vortioxetine (Brintellix) for the treatment of major depressive disorder (MDD). Brintellix is a novel antidepressant thought to work by enhancing serotonergic acitivty as a serotonin (5-HT) reuptake inhibitor and agonist of the 5-HT1A receptor, among other mechanisms.

The efficacy of Brintellix was established through six 6- to 8-week studies at doses ranging from 5 mg to 20 mg/day and one 24- to 64-week maintenance study in adults at doses of 5 mg to 10 mg/day. One short-term study of the 5 mg/day dose was in the elderly.

Brintellix is available as 5 mg, 10 mg, 15 mg, and 20 mg immediate-release tablets. The maximum recommended daily

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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. 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 October 31, 2014. As a subscriber to *TCPR,* you already have a username and password to log on www.TheCarlatReport.com. To obtain your username and password or if you cannot take the test online, please email info@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. Which of the following cholinesterase inhibitors is FDA-approved for the treatment of vascular dementia (Learning Objective #1)?
   [ ] a) Donepezil (Aricept)
   [ ] b) Rivastigmine (Exelon)
   [ ] c) Galantamine (Razadyne)
   [ ] d) No member of the class has an FDA indication for treatment of vascular dementia

2. First-line medications for the treatment of depression in dementia include which of the following (LO #1)?
   [ ] a) SSRIs [ ] b) Cholinesterase inhibitors [ ] c) MAOIs [ ] d) Tricyclics

3. Which type of dementia often has symptoms that include increased tone, tremors, and falls (LO #2)?
   [ ] a) Alzheimer's disease [ ] b) Lewy Body dementia
   [ ] c) Frontotemporal dementia [ ] d) Vascular dementia

4. According to Dr. Dan Blazer, an atypical antipsychotic is preferable to a typical antipsychotic in treating the elderly, and patients may be able to rotate on and off of them as needed (LO #4).
   [ ] a) True [ ] b) False

5. In the Le-Niculescu H et al study of suicidality, the most predictive biomarker identified was which of the following genes (LO #4)?
   [ ] a) *PTEN* [ ] b) *MARCKS* [ ] c) *SAT1* [ ] d) *MAP3K3*

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Expert Interview

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Dr. Blazer: A number of things have come out over the years, both from our research and the research from many others, to suggest that physical health is a key predictor of better aging, so exercise and watching one's diet are major factors. Cognitively, we've found that it's important to remain involved in interesting and useful things. When older adults keep involved with other people and with interesting ideas—through social interaction, reading, even going on Facebook—this can help greatly. In addition to that, studies show that individuals who endorse some form of spiritual well-being actually do better physically and emotionally.

TCPR: Thank you, Dr. Blazer.

Measuring Function in the Elderly

Dr. Blazer recommends the following easy-to-use activities of daily living scales to assess patients' function. They can all be found for free online.

- Katz Index of Independence in Activities of Daily Living (ADL)
- The Rosow-Breslau Functional Health Scale
- Older Americans Resources and Services (OARS) Activities of Daily Living (ADL) Scale

News of Note

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dose is 20 mg/day. Brintellix is contraindicated in people taking MAOIs, the antibiotic linezolid (Zyvox), or IV methylene blue. The most common side effects are nausea, vomiting, and constipation.

BRAIN RESEARCH

The Brain May Remove Toxins During Sleep

Scientists have discovered that the brains of mice clean toxins from between cells while they are sleeping. During sleep, the space between brain cells increases by about 60%, allowing the glymphatic system, or the brain's "plumbing" system, to flush the brain with fluid.

So called because it acts like the lymphatic system but is mediated by glial cells, the glymphatic system allows for the removal of waste products from cerebrospinal fluid (CSF). Researchers found that, while mice slept, brain cells shrank as CSF flowed through the brain parenchyma and ultimately into venous drainage. Past research has shown that toxins involved in neurodegenerative disorders accumulate between brain cells. In fact, researchers injected mice with beta-amyloid, a protein associated with

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Current Pharmacological Treatment of Dementia

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TCPR'S VERDICT: No pharmacological cure for dementia currently exists, but treatment options are numerous. Cholinesterase inhibitors and memantine are reasonable alternatives unless you strongly suspect FTD. Aim for the doses established by evidence rather than titrating dose to response. When adding medications, be sure to follow the basic principles: one medication change at a time, and "start low and go slow" with dose adjustments. Managing the expectations of patient and family is crucial. The patient should neither be left without hope nor given a false impression that a complete turnaround of symptoms is possible.

News of Note

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Alzheimer's disease, and found that it disappeared faster in the brains of mice who were sleeping than those who were awake.

The results of this study show hope for further understanding and treating neurodegenerative diseases, including Alzheimer's disease. The study can be found in the October 18 issue the journal *Science* (Xie et al, *Science* 2013;342(6156):373–377).

Next month in *The Carlat Psychiatry Report*: Depression

This Month's Focus:
Treatment of Dementia

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