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Shirley M. Neitch Marshall University, neitch@marshall.edu

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# Standing in the Gap: The Primary Care Physician and Alzheimer's Disease

#### Shirley M. Neitch, MD, FACP

Professor of Medicine and Chief, Sections of General Internal Medicine and Geriatrics, Department of Internal Medicine, Marshall University/JCESOM Medical Director, WV Alzheimer's Outreach and Registry Program, Blanchette Rockefeller Neurosciences Institute at West Virginia University

### Introduction

An astonishing volume of material has been published about Alzheimer's disease in recent years. Typing the word "Alzheimer's" into Google will reward you with 13,600,000 "results" in 0.15 seconds, and a PubMed search of the same instantly yields over 55,000 journal articles. Yet, primary care physicians (PCPs) who regularly see patients with Alzheimer's and related dementias know that huge gaps exist in our knowledge and our ability to provide optimal care.

Neurologists, geriatricians, and psychiatrists may be perceived as the physicians who most often care for Alzheimer's patients, but there is no doubt that it is generalist PCPs who are providing the bulk of the care of Alzheimer's patients. In a survey of PCPs in West Virginia conducted by the Outreach Program of the Blanchette Rockefeller Neurosciences Institute (BRNI) in mid-2009, 99% of respondents said that they see at least one patient per month with Alzheimer's disease or a related dementia, and a full 31% said

that they see 16 or more monthly. Demographics alone make it likely that virtually every PCP in the state will see more than four Alzheimer's patients monthly, as there are perhaps 46,000 victims in WV, and approximately 1600 practicing PCPs available to take care of them. This review is intended to provide PCPs with a practical, evidence-based framework for approaching the many affected patients who will come to their offices – a way to stand in the clinical gap while scientists work furiously searching for the cure.

# **Recognition and Screening**

Because dementia is by definition an indolent disorder, recognition of it is a challenge in primary care offices, where the focus is often, of necessity, one of rapid assessment and speedy decision-making. The fact that patients may have been seeing the same physician for years is potentially both a help and a hindrance in discernment of the subtle findings which signal the onset of a dementing illness. These changes might be more readily apparent in familiar patients, in whom PCPs may find the new presence of a memory disturbance to be relatively obvious; however, when a primary care physician has become accustomed to looking at a particular set of problems in a particular patient, one might not even notice the onset of the typically very nuanced early signs of dementia. So, it is worthwhile for PCPs to consider a defined set of warning signs or clinical hints that a patient may be in the early stages of dementia.

The Alzheimer's Association has recently published an updated version of their "10 Warning Signs", a useful document for PCPs to review and consider posting in their offices. (This can be downloaded from www.alz.org.) Widespread public dissemination of this list will help families and patients themselves to decide when they should inform their physician of concerns about memory. A few other clinical warning signs may not be as immediately recognized as heralding dementia, but should also be heeded by physicians. These include:

- The Poor Historian: This timehonored description of the patient who just can't seem to tell a coherent story about their medical history may serve as be a red flag; if a PCP is tempted to note this as a feature of a patient's presentation, a follow-up question should always be asked - "Could this be due to early dementia?"
- The Repetitive Caller: If the front desk staff notices that a patient has called several times to check on some aspect of an appointment, or if the nurse

# **Objectives**

There is a huge volume of information recently published about Alzheimer's disease, but most of it is not targeted to the average busy primary care physician, even though these PCPs are providing the bulk of care to patients with dementia. This paper is a succinct clinical review of the current state of diagnosis and treatment of Alzheimer's disease, including citations of resources for physicians and caregivers.

- reports that the patient called multiple times for a refill, the physician should "file" this information, perhaps even literally put a note in the chart so it can be considered at the patient's next appointment.
- The Unexpectedly Delirious
   Patient: Delirium, especially
   occurring with a relatively
   minor physiologic insult, may
   presage the onset of dementia.
- The Patient with a New Best Friend: Persons with dementia are easy targets for those who would exploit them, for monetary or other purposes. When a patient inexplicably appears at the office with someone who claims to have befriended them or to have begun "helping" them, for no obvious reason, the clinician would be wise to maintain a level of skepticism.

Once a problem is recognized, the PCP should screen the patient with a standardized instrument to ascertain if the problem is a true memory disorder. "Screening", in terms of community events or widespread screening of asymptomatic individuals, is not recommended.1 Home screening is particularly discouraged. However, office-based case finding is a necessity, and can be accomplished with relatively little time commitment and without disruption of office routines. A multitude of screening instruments have been developed and are available, but the clinical utility of many of them is limited by the amount of time or expertise required to do the testing accurately. The WV Alzheimer's Outreach and Registry Program (AORP) recommends that PCPs use the "Mini-Cog" screening tool. Briefly this consists of a three word recall test and a clock drawing exercise, which can be performed by any trained person in the office (MA, nurse, or physician), and has been

# Table 1. The "Mini-Cog" Screening Instrument

#### The test:

Give the patient a list of three simple words. (Example: "ball, flag, tree" - or - "apple, penny, table") Ask the patient to repeat the words so you will know they have been heard and understood. Perform a Clock Drawing Test. Ask the patient to: draw a circle; put in the numbers as on the face of a clock; put in the hands of the clock to show a particular time. (Choose a time in which the hands of the clock are fairly separated, but not an "easy" time such as 3:00 or 6:00.) Ask the patient to recall the three words.

# The scoring:

- One point for each word recalled (without prompting)
- One point for normal clock, zero points for abnormal clock. (It is your judgment call as to whether a clock is normal.)
  - o Three or four points not supportive of dementia diagnosis
  - o Zero to two points supportive of dementia diagnosis

demonstrated to require only about three minutes to complete.<sup>2</sup> (Table 1)

# **Diagnosis**

If a screening test indicates a possible dementia, the next step is to attempt to firm up a diagnosis. There is significant overlap in the clinical presentation of Alzheimer's disease, vascular dementia, and certain other common dementias, and often a patient may have a mixed disorder. PCPs realize, and must make it clear to the patients and families, that no clinically useful test currently exists which will unequivocally confirm a diagnosis of Alzheimer's disease. Certain tests are necessary, though, to rule out other causes of dementia, some of which may be partially treatable.

While the history and physical examination are critical, findings may be non-specific; particularly important features are noted in Table 2. Likewise, laboratory testing need not be extensive, but certain critical tests must be obtained. (Table 3).

Imaging is recommended by the American Academy of Neurology.<sup>3</sup> Depending on what is most readily available in the area, and what other

clinical issues may be present in the patient, CT or MRI of the head may be ordered. Either will rule out certain other unsuspected pathology, and can help define the extent of vascular changes. PET scanning, with either FDG (glucose utilization functional scanning) or with "Pittsburgh Compound"/ PIB (which

Table 2. Physical Examination Features of Alzheimer's Disease

PE may be, and often is, completely normal. Potentially abnormal findings include:

- Anosmia
- "Bewildered" affect, especially in later stages
- Failure of "One-Leg Standing" test [cannot stand 5 seconds on one leg]
- Numerous "subtle neurologic abnormalities" [the presence of subtle findings which are non-diagnostic in and of themselves, including: generally diminished DTRs, decreased grip strength, pronator drift, etc.]
- Various speech abnormalities involving content or fluency

### Table 3. Testing Needed in the Evaluation of Possible Alzheimer's Disease

There is no clinically useful diagnostic test for Alzheimer's at this time, but several tests should be done to rule out other memory-loss disorders:

- Complete Blood Count; Complete Chemistry Profile
- Thyroid Function Tests
- B12 levels
- Neuroimaging CT Scan or MRI of head
- Depression Screening

binds to amyloid), yields imaging which best discriminates among Alzheimer's and other dementias, and is the imaging modality which comes closest to being a "diagnostic" test. However, many insurance carriers consider it to still be "experimental", and therefore they will not cover it. Medicare covers PET scanning for dementia diagnosis only within the strict boundary of testing to differentiate between Alzheimer's and Fronto-Temporal Dementia, and only after documentation of

decline in mental status scores over six months or more.

Other evaluation/diagnosis strategies are under development, including a skin biopsy technique now being studied at BRNI. The NIH is involved in a wide-ranging study of neuroimaging, which likewise is very promising but as yet is not complete enough to yield definitive recommendations.

#### **Treatment**

Once the PCP is comfortable with a diagnosis of Alzheimer's,

treatment must be considered, and generally, three aspects should be addressed – risk factor modification, treatment of the disease, and treatment of behaviors. (Table 4)

# **Addressing Risk Factors**

Prevention of Alzheimer's cannot be guaranteed at this time, because we simply don't know enough about the pathophysiology. The best defined risks are roughly the same as the known risk factors of atherosclerotic disease, including hypertension and hypercholesterolemia. Recently it has been more clearly shown that diabetes mellitus4 and heavy smoking<sup>5</sup> in mid-life are independent AD risk factors. Attempting to modify Alzheimer's risk factors once the disease is manifest, in an attempt to change the course of the Alzheimer's itself, may be considered futile, and at this time in history, it probably is. However, for



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Table 4. Treatment Approaches for Alzheimer's Disease

### Disease-specific rx:

Cholinesterase Inhibitors (CHEI)

Donepezil (Aricept™)	Once daily dosing; long clinical experience
Rivastigmine (Exelon™)	Available in transdermal patch
Galantamine (Razadyne™)	Multiple dosing options

# NMDA receptor blocker

1	B.A. (' /B.I. I. TM\)	la il a Guerra i a
	Memantine (Namenda <sup>™</sup> )	l Add-on to CHEI in late stages
1	Wemantine (Namenga¹™)	I Add-on to Chel in late stades
1	, , , , , , , , , , , , , , , , , , ,	riam on to one in the stages

#### Treatment of adverse behaviors:

Always attempt non-pharmacologic approaches first.

Various medication classes may have a role in specific cases, including antidepressants, anti-anxiety agents, antipsychotics. Must be tailored to patient and closely observed.

#### Risk factor modification:

Treatment indicated for primary risk factors including hyperlipidemia, diabetes, hypertension, *but* "tight" control, especially of diabetes, should be avoided once the dementia is clinically manifest.

Head protection, via fall avoidance and seat belt use, should be emphasized.

patients in early stages of the disease, modest attempts to control risk factors are reasonable. Good control of hypertension is worthwhile, and attaining some control of hyperlipidemia and diabetes may be useful. "Tight" control of diabetes is not indicated due to the risk of hypoglycemia, which itself is a significant contributor to dementia. Protection of the head by use of seat belts and assistive devices for ambulation should be continued, for as long as the patient can cooperate. Sepsis confers a three-fold increase in the risk of subsequent cognitive impairment, and so should be aggressively treated.6

#### **Disease Treatment**

Treatment of Alzheimer's Disease itself can be attempted with two categories of drugs. The cholinesterase inhibitors have been available for several years and remain the first line choice for treatment. These include donezepil,

galantamine and rivastigmine. The second available medication is the NMDA receptor blocker menantine, which is recommended as an add-on to treatment with a cholinesterase inhibitor. Outcome of treatment with these agents is variable, with an occasional patient showing visible improvement, but for the most part they are given in hopes of slowing disease progression. While there is still a great deal of controversy as to the true benefit of these medications, they are currently all we have to offer, and most patients and families will want a trial of treatment.

# **Treatment of Behaviors**

Non-pharmacologic approaches to controlling adverse behaviors must always be attempted before drugs are used. Often, improving caregivers' understanding of why patients behave the way they do may forestall the need for medication. The Alzheimer's Association is an excellent resource

for those seeking information about these non-drug approaches.

Occasionally, however, all attempts at non-drug therapy will fail, and consideration will have to be given to using psychotropic medications. PCPs who find themselves needing to prescribe such medications in demented patients should first be sure that they are treating the patient and not the caregiver. If a behavior, hallucination/delusion, or sleep disturbance is not a problem for the patient, it requires no treatment. If the patient is endangered, though, by their own behavior, then treatment will be necessary, and the PCP will have to determine which therapeutic class to use based on their in-depth knowledge of the patient. Occasionally benzodiazepines, antidepressants, or mood stabilizers will have a place in treatment; occasionally there are no options left except antipsychotics. Of course there are black-box warnings

on these medications now, if they are to be used in dementia, and many physicians feel that informed consent is necessary.

A recent meta-analysis supports the use of cognitive interventions for both behaviors and cognitive/ intellectual decline.7 The interventions which have worked, however, are specific therapies administered by professionals, such as "spaced retrieval techniques" and "sensorimotor skill stimulation", not the simpler games and puzzles often recommended or marketed for this purpose. PCPs should inform patients and families to remain engaged with various activities, but should discourage purchase of special software or games.

# **Caregivers**

Most of the care of Alzheimer's patients is provided by unpaid family caregivers, and very often the care must be given full time, with little respite for the caregiver. The adverse outcomes of caregiver stress are well known, and their needs must not be overlooked. The WV Bureau of Senior Services has two programs that may be beneficial for those who qualify, "Lighthouse" and "FAIR",

but the programs are underfunded, and cannot provide services to nearly all who need them. Again the Alzheimer's Association, and also the WV chapter of the National Family Caregivers Association (www.thefamilycaregiver.org) may be useful resources.

#### The Future

Much scientific work is underway as we seek a cure for this devastating disorder. West Virginia is privileged to be home to the Blanchette Rockefeller Neurosciences Institute, the only privately endowed facility in the nation devoted to researching this disease, where currently numerous studies are underway regarding pathology, diagnosis, and treatment. An Alzheimer's Registry is also under development at BRNI. PCPs will use this more than any other group of practitioners and BRNI will be providing extensive education prior to the registry being fully implemented.

Additionally, though, our societal commitment as a nation must improve, because currently, for each cent that the NIH devotes to Alzheimer's research, we spend

\$3.50 on the care of persons with the disease.<sup>8</sup> As the nation ages, the prevalence of Alzheimer's will continue to increase; we simply must have more research on both prevention and cure.

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# **CME POST-TEST**

- 4. Which statement is true regarding screening for dementia?
  - a. Large community-based screenings at health fairs are very useful and easy to do.
  - b. Case-finding, with standardized assessment tools, can be done in a primary care office without disruption of patient flow.
  - c. Screening is not necessary, as the diagnosis is always obvious soon after onset of the disorder.
  - d. The most efficient screening tool is the ADAS-Cog.
- 5. Two categories of drugs are currently on the market for treatment of Alzheimer's Disease. Of the two, the one recommended for an initial treatment trial is:
  - a. ACE Inhibitor
  - b. NMDA receptor blocker
  - c. Cholinesterase inhibitor
  - d. Antioxidant
- 6. Special software, games, and activities are currently being marketed as tools for both cognitively normal persons and early dementia patients to use to maintain or improve memory and cognitive flexibility. These items are:
  - a. Strongly recommended as proven and reliable
  - b. Too simple for even the average Alzheimer's patient
  - c. Equal in effectiveness to cognitive interventions performed by professional therapists
  - d. Not as effective as specific therapies such as sensorimotor skill stimulation.