

# NORMAL AGING, MCI AND THE DEMENTIAS

NOTE TO READER: The six chapters in this section are draft chapters that will appear, in a year or so, in our new book, Mild Cognitive Disorders. Your comments and recommendations are welcome. You may cite them as you please by referencing our website. The reference lists are available from the author..

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In the next 6 chapters, we shall address clinical and theoretical aspects of normal aging, Mild Cognitive Impairment and the various dementias. Of all the sections in this book, these topics are the most important; of all the topics, this one touches us all.

A word on terminology. “Mild Cognitive Impairment” or “MCI” is used to refer specifically to the intermediate state that resides somewhere between normal aging and dementia. In dementia studies, MCI is dealt with as a form of preclinical dementia, and it often is. But the term itself could just as well refer to any of the conditions discussed in this book. To avoid confusion, we shall try to avoid using the term in a non-specific way, and when we do, we shall not use caps. When caps are used, or the acronym MCI, we are referring to the condition as Petersen intended.

A word about Alzheimer’s disease (AD): we distinguish between Alzheimer’s pathology, which is virtually ubiquitous among the dementias, as well as in normal aging; and Alzheimer’s *disease*, which is AD pathology accompanied by clinical expression, that is, disabling and progressive cognitive change.

We use the term *dementia* to refer to the functional state of cognitive disability, regardless of cause, as long as the cause is a progressive condition. In some circles, the term dementia is still used to refer to severe cognitive impairment caused by trauma, hypoxia, encephalitis, etc. It is not inappropriate to the outcome of a static encephalopathy as dementia (as in “dementia secondary to traumatic brain injury”), but we prefer not to. We shall apply the term only to conditions characterized by progressive neurodegeneration.

Since AD is the prototypical form of dementia, the points we make concerning AD are, more often than not, true of other dementing conditions. The reader should understand that is the case from the context of the discussion, but ambiguity may occur. It is just too clumsy to write “AD and the other dementias” over and over.

The first chapter is concerned with normal aging, or benign senescence. “Benign senescence” refers to the cognitive and behavioral correlates of normal aging. We shall trace the neurocognitive changes that begin sometime during the fourth decade of life and that continue on a downward course thereafter. We shall also describe the changes that happen to brain during the course of normal aging. The involution of nervous tissue is an inevitable accompaniment of aging, and it is upon this matrix that aging-related diseases work their ill effects. Aging is not a disease any more than dementia is normal, but unless one understands the “pathology” of normal aging, the study of dementia will be all that more ambiguous and imprecise.

The second chapter addresses the “problem of dementia” in terms of the interactions of three complex functional systems. Low education is asserted to be a “risk factor” for the development of dementia. Our opinion is that intelligence is central to the education effect. Education is thought to be

protective because it increases synaptic density, or “brain reserve.” In fact, the biological correlate of intelligence – synaptic efficiency – is a more cogent explanation, and it speaks to the integrity, or resilience of the higher cortical functions. Intelligence is not only protective against dementia, but also against cardiovascular disease and mortality. It is an index of the integrity of complex functional systems in *soma* as well as *psyche*.

Emotional self-regulation is another complex functional system that seems to be awry in people who are predisposed to develop AD in particular and probably dementia in general. That is why depression, anxiety and personality disorder appear in some studies to behave as “risk factors” and in others as early symptoms of dementia. The relative integrity of the cardiovascular system is another participant in one’s proclivity to develop dementia; it, too, is influenced by IQ and by the subject’s capacity for “distress control.”

The arguments in the second chapter are a “logical box,” or a framework for understanding the problem of dementia in qualitative terms. Aging and dementia are complex phenomena that incorporate three processes: the gradual winding-down that characterizes all complex systems; the integrity, or resilience that is built into every successful system; and the pathology that interacts with the first two processes.

In the third chapter, we shall address the problem of dementia screening, which we think is a good thing, although we acknowledge some arguments to the contrary. Not surprisingly, we propose that computerized testing is the best way to go about universal screening; that it should begin sometime between age 40 and 50; and ideally should be a routine part of one’s annual medical examination. It is a well-documented fact that dementia is not likely to be discovered by primary care physicians until the condition is well-entrenched. By the time such patients are referred to neurologists, they are impaired, indeed. Current practice is not conducive to early diagnosis, and that probably has an impact on the success of our treatments.

The problem with computerized testing is that it is so sensitive. It can pick up MCI at the very earliest stages, but it also generates a formidable problem with false positives. It is our opinion that MCI is not a diagnosis, in the conventional sense of the term, but, rather, the occasion for a differential diagnosis. That is the topic of the fourth chapter. The differential diagnosis includes ADD and the learning disabilities, old brain injuries, and a host of different encephalopathies. Drug effects and psychiatric disorders, which can also lead to mild cognitive impairment (note: no caps) are dealt with elsewhere in this volume.

In the fourth chapter, we also discuss the different screening tools that are used: brief tests, like the MMSE; questionnaires and rating scales; neuropsychological tests and computerized test batteries. Our position, as we said before, is that computerized tests are the best approach to the problem. Two computerized test batteries are commercially available, NeuroTrax® and CNS Vital Signs®. The author is one of the developers of CNS Vital Signs, and many of the data we present in the chapters that follow are taken from studies we have done using that instrument. I shall not take offense if the reader approaches these data with a degree of caution, since I have an abiding interest in the success of that test battery. In fact, my colleagues and I do not believe that computerized testing is an ideal way to approach the problem of dementia screening because we developed CNS Vital Signs. Rather, we developed CNS Vital signs because we believed that computerized testing is an ideal approach, and were dissatisfied with the computerized batteries that existed, at the time.

In the fifth chapter, we deal with dementia diagnosis: the medical tests that are usually recommended as part of the workup of a patient with MCI or early dementia. The stated goal of the dementia workup is to look for reversible causes of dementia. An additional purpose is to establish the etiology of the condition. The latter is something of a preoccupation to academic physicians and

researchers, and it is a worthy exercise. But PET scanning, CSF testing and genotyping have little utility in terms of management, and are rarely done, outside of research centers.

The sixth chapter has to do with dementia prevention and treatment. We understand that “there is no evidence that any intervention can prevent the onset of dementia.” But there are lifestyle and dietary changes that people can make that may delay the inevitable, or at least let them feel that they are doing so. The various dietary supplements, vitamins and medications for which claims of protection are made are dealt with critically, but sympathetically. Most achieve the grade of C – “speculative but not outlandish” – but there are a few B’s. Finally, we discuss the “active treatments”: the cholinesterase inhibitors, NMDA antagonists, stimulants and antidepressants. They are probably not “disease modifying” drugs, but they might be more effective if we used them earlier in the course of the disease.

I end on this note, a system that I think is reasonable and practical:

- Computerized neurocognitive testing should be routine for all patients, on an annual basis, beginning in their 40’s, when most people start getting annual physical examinations. This gives every patient a baseline against which future changes can be measured. It also will identify MCI at the earliest possible moment.
- Conservative protectives for every patient over 50: fish oil, low dose aspirin or ginkgo and a multivitamin.
- Identify patients at the earliest stage of MCI by using computerized tests, and by recognizing these factors: family history of dementia, cardiovascular risk including homocysteine and other inflammatory markers, depression, anxiety, rigidity, personality change.
- Consider aggressive prevention for patients at risk: anti-inflammatory doses of aspirin or other NSAIDs, a statin, perhaps also a “cocktail” of antioxidants.
- A low threshold to use stimulants and antidepressants for mild problems with energy or depression in elderly patients. A vigorous approach to antidepressant treatment if the patient has residual depression.
- A cholinesterase inhibitor (ACI) and/or an NMDA antagonist, certainly as soon as there is evidence that a patient at risk is beginning to decline, but preferably earlier
- Lifestyle modification and optimal cardiovascular health for everyone. A Mediterranean diet, red wine, green tea, a lot of fruit and vegetables, vigorous physical and mental exercise.