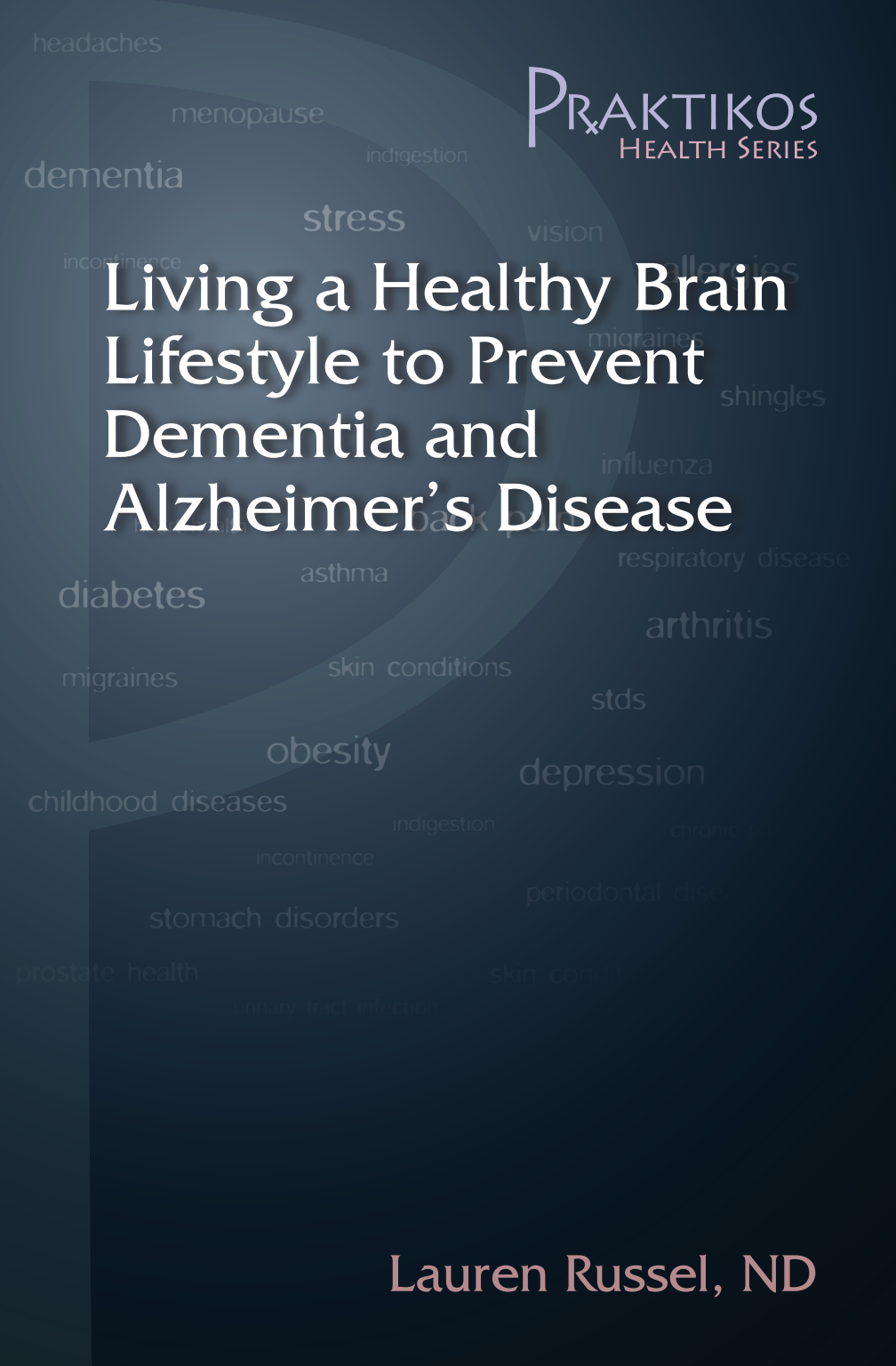

PRAKTIKOS
HEALTH SERIES

Living a Healthy Brain Lifestyle to Prevent Dementia and Alzheimer's Disease

Lauren Russel, ND

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Praktikos Books
PO Box 457
Edinburg, VA 22824
888.542.9467 info@praktikosbooks.com

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Preface

A diagnosis of Alzheimer's disease or any other cause of dementia that would shorten your cognitive lifespan is very frightening. While we hear so much about this disease, many of us may not understand what it is and what some of its early warning signs are. What is even more alarming, many of us do not know some of the simple things that can be done to prevent or reduce risk factors years before it occurs, mostly because there are very few actually talking about what can be done.

This book will tell you what dementia is, some of the things that contribute to it, and what you can do now to prevent or stall its progression. If you have a friend or loved one with Alzheimer's, they may benefit from some of the information to be covered.

As of this writing, two problems remain true in the approach to dementia and Alzheimer's disease. First, medical research lacks a good way of making an early diagnosis in those most susceptible to its development. Second, once identified, there are few known effective therapies to halt its progression. This does not mean that there is nothing that can be done to forestall progression of these diseases, however.

There is a large body of evidence from scientific studies suggesting that the most effective strategy to date for preventing Alzheimer's disease and dementia is modification of lifestyle and risk factors. There are many ways of doing just that.

Introduction

The Emerging Picture of Alzheimer's Disease

MOM USED TO LOVE to be with her family, but now she seems so distant and quiet. She often doesn't remember names or faces and doesn't participate in activities she used to enjoy. Frequently, she becomes lost just walking around the block. Her husband, a devoted and supportive partner, doesn't know what to do to help his wife anymore. The woman who was once so independent and resourceful seems to be disappearing day by day and the whole family feels helpless.

The sad thing is that none of the conventional doctors seem to know what to do about it, either. Their only solution is expensive drugs that seem to cause more harm than good or forestall the inevitable. It's only a matter of time before Mom will need

constant care in an assisted living facility or nursing home. Everyone is dreading that day.

Does this sound familiar? Is it a scenario affecting your siblings, your spouse, or quite possibly, you? Do you fear that your body will outlive your brain, leaving you with precious little of the life you have built and the family you have cherished?

When you have Alzheimer's disease or other types of brain changes causing memory loss, your mind gradually slips away and you don't remember the important things that have made you "you." You lose the life you once had, including all the memories and connections that created the complex tapestry of your life. It's all the more alarming because you have little warning that it's occurring until the symptoms are obvious to others. The intellectual function that you relied upon daily is gone, replaced by changes in your ability to do and remember simple things. The memory loss that you experience will gradually be accompanied by emotional changes and even physical limitations as the disease progresses.

A Global Problem

The question we all ask ourselves whenever we lose our keys or have a momentary lapse in remembering a name is, "Do I have Alzheimer's disease?" It's a scenario we all dread. At the same time, it is a real problem facing each of us and there is not a

moment to lose in unraveling the issues that face us as our brains age.

Alzheimer's disease and abnormal brain changes occurring with age are a problem of global dimensions, affecting people all over the world. Some call it a problem of epidemic proportions, with just a few precious years left in which to find solutions before governments and care facilities are bankrupted and overrun with the many millions needing help. Currently, forecasters estimate that more than 14% of those over the age of seventy are affected by Alzheimer's disease and dementia, with this number projected to increase to as high as 50% over the age of eighty-five.[1]

Worldwide, more than 26.6 million people are affected by Alzheimer's disease and dementia. A recent study by the Johns Hopkins Bloomburg School of Public Health predicted that this number would increase to 106 million worldwide by the year 2050 and affect one in eighty-five people globally.[2] By 2050, this number may grow to sixteen million in the United States alone.[3] The cost of caring for those who have Alzheimer's disease is estimated to increase from $200 billion a year in 2012 to $1.1 trillion in 2050 (based upon today's dollars), a cost that is not economically sustainable. Up to 70% of these costs are borne by Medicaid and Medicare.[4]

Alzheimer's disease and dementia are health problems affecting more than just those with the

disease. The Alzheimer's Association predicts that there are currently nearly fifteen million people who provide uncompensated care to people with dementia-related illnesses. Dementia and Alzheimer's disease are conditions that dramatically change families, increase stress, and adversely affect the health of those caring for those they love. Surprisingly, of the 800,000 single individuals living with Alzheimer's disease in the United States, at least half of them have no one identified as a caregiver. This group, which includes many single older women, is at great risk from the deficiencies of cognitive impairment as well as malnutrition and under-treatment of medical conditions.[5]

The tragedy of Alzheimer's disease and dementia is compounded by the loss of memory, quality of life, and ultimately, the ability to function when the brain ages in this way. Alzheimer's disease and other age-related dementias are on their way to becoming some of the most significant causes of death, exceeding those of heart disease and cancer. While death rates for many diseases affecting older Americans continue to decline as helpful therapies are identified, death rates from Alzheimer's disease are increasing. Right now, Alzheimer's disease is the sixth leading cause of death in the United States. It's not only a leading cause of death, but responsible for shortening the lives of Alzheimer's patients, who generally live only about eight years after diagnosis.[6]

No known treatment exists that stops the onset of, or, once identified, retards the progression of Alzheimer's disease. Researchers are intensely focused on finding ways to identify early Alzheimer's disease and other forms of dementia, with the hope that this will reduce the numbers who progress to overt disease. Even a small reduction in onset and progression can have a significant impact globally. Simple interventions could eliminate 9.2 million cases a year, especially among those needing the highest level of care.[7–9]

What does this mean for each of us, individually? It can mean many more years of healthy brain aging . . . and not having to lose loved ones to this disease that spares the body and destroys the brain.

Why Conventional Medicine Cannot Fix the Problem of Dementia and Alzheimer's Disease

Science has led us to believe that dementia, Alzheimer's disease, and cognitive decline are aspects of normal aging. The truth is that these are symptoms of abnormal aging in most cases.[10,11]

One of the biggest "myths" being marketed by pharmaceutical companies and other researchers who stand to profit is that they are going to be able to fix the problem of abnormal brain aging using drug therapies designed to correct "chemical imbalances"

in the brain. Pharmaceuticals are being designed to slow the effects of dementia, rather than finding ways to prevent abnormal brain aging using natural therapies and common sense approaches. The misconception is that the brain changes that are observed in Alzheimer's disease are caused by the accumulation of plaque and tangles formed from amyloid beta and tau proteins rather than damage from the effects of imbalances, lifestyle choices, and environmental exposures to processes affecting the learning centers of the brain.

Most drug therapies are designed around the theory that acetylcholine, a neurotransmitter, is reduced in the brain and that drugs will increase it, improving symptoms of dementia. The problem is that most therapies are very short-lived—palliative at best for three–six months—and often cause liver damage in the process. In addition, they rarely change the progression of Alzheimer's disease.

Many of these drugs have significant side effects, causing additional health challenges and do not seem justified considering that very few show significant improvement from any of the drug therapies.

Sadly, conventional treatment often includes antipsychotic and antipsychotropic medications. While nearly half of all people who have dementia living in assisted living and nursing homes are on these drugs, they are often inappropriate for the illness and frequently fatal. Many will die pre-

maturely because of the adverse effects of these drugs. When on them, a patient's quality of life is severely affected, reducing their ability to communicate, increasing confusion and brain fog, and decreasing cognitive function.

The antipsychotic medications most commonly used are Zyprexa® (olanzapine), Seroquel® (quetiapine), and Risperdal® (risperidone). While they are given to reduce symptoms such as delusions and aggression, experienced by up to 75% of Alzheimer's patients, most people do not experience much benefit in relation to the significant side effects they can cause, including sudden death.[12–14]

More recent research—conducted by independent agencies that do not stand to benefit from the results—shows little or no benefit from drug therapies to control neuropsychiatric symptoms and are, in fact, associated with significant adverse events.[15,16]

Since dementia is a multi-factorial disease with a wide constellation of symptoms, drug therapies must also be directed toward treatments that take each of them into account. Treating the decline of mental function may increase stroke or cardiovascular risk. Therapies are needed to treat underlying disease processes, in addition to the dementia. Each of these approaches has an impact on cost, compliance, and poses potential risk from drug interactions.[17]

There are many people who now believe that there is not going to be a cure based on any drug therapy and that money and efforts should be directed toward prevention and elimination of risk factors.[18–20]

New Ways of Thinking about Brain Aging and Dementia

In fact, one treatment approach has had some success in taking those with Alzheimer's disease and dementia off all of their medications with remarkable results. This approach is outlined in the book, *Contented Dementia* by Oliver James, which describes the efforts of Penny Garner, founder of SPECAL (Specialized Early Care for Alzheimer's). The book outlines the specialized approach to care that was developed by Penny in which caregivers support the individual's long-term memory, usually intact in Alzheimer's patients, along with an emphasis on positive emotions and feelings. When it's pointed out to someone with dementia that they've forgotten something, they often become embarrassed and agitated. By focusing on what a patient remembers and supporting that happy, contented feeling, patients feel better and do better, leading to reduced medical costs and a decreased need for medications to control agitation.[21]

To see what is going on in the development of the different types of dementia, it's useful to

examine normal brain aging and those things that can occur to set it off track.

1

What is Normal Brain Aging?

NORMAL BRAIN AGING IS the process of getting older but remaining mentally functional. Even in the absence of disease, the brain ages and cognitive changes occur very slowly. Researchers are beginning to understand that parts of the brain communicate less effectively in adults in their seventies and eighties than they do in adults in their twenties.[22]

While there may be a slowing of some skills and a reduced processing speed, in general, mental skills should remain intact for a lifetime.

There is no "normal" diminishment of skills in the healthy individual. In fact, a new study showed that elders responded as accurately but more slowly

and with more care on simple tests when compared to college-aged students. The slower speed of the elders on testing was due to an emphasis on accuracy rather than speed of response. What was clear from the study was that older individuals had brain-processing speeds similar to those of the younger people but responded more slowly because they wanted to be accurate on the tests. When encouraged to go more quickly on testing, the elders were able to do so and their reaction times became similar to those of the college-aged students.[23,24]

These types of studies show that our perception of aging is incorrect and that normal aging does not necessarily mean a decrease in mental or cognitive skills.

When cognitive changes do occur with aging, however, they are not reflective of normal aging at all, but are the result of a buildup of neurodegenerative lesions that we now associate with dementia, something that has been suspected by some researchers for a long time.

That memory changes are not a normal part of aging was very recently demonstrated in a long-term study known as the Religious Orders Study. The 354 individuals in the study were given cognitive testing over the course of thirteen years, with many donating their brains for assessment upon their deaths. Cognitive testing was done at the beginning of the study and throughout the thirteen years of follow-up.

As they followed these individuals over time, researchers discovered that mild cognitive decline was actually associated with tangles and lesions in the brain. When tangles were found to be very low or nonexistent in the brains of participants at autopsy, it was highly correlated with no change in mental function. When the density of tangles increased or were significant at autopsy, then there had been significant change in cognition over time.

However, even with low tangle volume, there were changes in cognition noted related to disease processes occurring within 52 months of death (a time frame artificially derived for study parameters), at which researchers concluded there were other types of pathology occurring that had an impact on progress toward dementia. When brain changes were suggestive of Alzheimer's disease, the impact was more severe.

The conclusion made by study authors was that, "the neurodegenerative lesions traditionally associated with dementia are principally responsible for the gradual age-related cognitive decline that precedes dementia and that Alzheimer's disease and related disorders have a much greater impact on late-life cognitive functioning than previously recognized."[25] Other authors have come to the same conclusions.[26]

There are, however, individuals who have evidence of plaque and tangles upon autopsy and yet

had no diminishment of mental function in their lifetimes. That is why many within the aging and Alzheimer's communities are trying to establish guidelines for appropriate diagnosis and assessment. It is an attempt to diagnostically separate those with symptoms of Alzheimer's disease and neurodegenerative changes from those who have few to no symptoms even though they have pathological changes in the brain.[27]

Looking into Your Medical History for Clues

Physical changes and diminishment of skills could be findings that encourage physicians to look deeper into a patient's medical history for clues. A recent study monitored 125 volunteers over the course of eight months and found that, in otherwise mentally and physically healthy older adults, falls may be an early warning sign of Alzheimer's disease. An increase in the number of falls may indicate a change in motor skills that are present before cognitive changes are detected. Using positron emission tomography (PET) imaging, researchers examined the amount of amyloid beta—a protein found in the brains of those who have preclinical (early and usually symptom free) Alzheimer's disease—and found that in those with amyloid beta present, there was a fall rate of 66% as compared to volunteers without much

amyloid burden. The fall rate was only 30% in those without much amyloid burden.[28]

The longer life expectancies for men and women over the last century have unmasked dementia—and Alzheimer's disease in particular—as one of the most common causes of intellectual failure. Dementia and Alzheimer's disease are, in truth, more of a "brain poisoning" than a normal aspect of growing older.

Processes that increase your risk of dementia begin many years earlier according to many researchers, making it more important that you establish good health habits early in life. According to a study by Duke Medical Center, more than one in three individuals over the age of seventy currently has some degree of memory loss without dementia because of coexisting medical conditions, such as diabetes, hypertension, stroke, and cardiovascular disease.[29] Progression to dementia from this group is estimated to be about 12% per year.

As science has come to understand more about diseases of abnormal brain aging, researchers have been surprised that brain changes leading to memory loss in patients may start occurring as much as twenty years before overt symptoms of dementia and Alzheimer's disease are apparent.[30–32]

Researchers now conclude that co-existing health problems may not only increase the speed with which brain changes occur but can lead to dementia much sooner than previously

thought. Some physicians are beginning to speak of "inflammation" as the underlying cause of dementia and other cognitive changes, creating a progression of physiologic changes—poor diet leading to obesity, diabetes and vascular changes predisposing to heart disease, stroke, and eventually some form of cognitive decline.[33]

Having hypertension at the age of fifty-four, for example, predicts changes in the size of the brain that can then be associated with problems with function as early as age sixty-one. Those who are carrying the APOE e4 gene, a major genetic risk factor for developing dementia, have an even greater risk of decline in mental function at an earlier age,[34] particularly when other health challenges are present.

Even a health condition like chronic kidney disease, which seems unrelated to the development of dementia, may be a risk factor for dementia development. In a research study of nearly 500 patients with chronic kidney disease, defined as a kidney filtration rate less than 60 mL/min for three or more months, dementia risk was increased independent of age, gender or any other health issues. It's suggested that, because chronic kidney disease is associated with heart risk factors and may increase oxidative stress in the body, it may be this mechanism that increases dementia risk.[35]

By the time symptoms of dementia appear, huge numbers of neurons have died. If efforts

were focused on prevention of the risk factors that begin the brain aging process, fewer people would develop mental impairment. The benefit to families and public health would be enormous, saving scarce financial and community resources.

Essentially, then, it is clear that drugs are not the answer. Our scientific efforts in the coming years need to be focused on early detection and adjustment of risk factors. As one researcher has put it, we need to focus on "neuroprotection" to ward off the changes that occur in the neurons as a result of our lifestyle, environment, and toxic exposures and prevent or slow down the synaptic changes that occur. Simple changes like increasing exercise, getting more and better sleep, and starting prevention efforts early enough to retard the appearance of symptoms may go a long way toward stopping this challenging and seemingly limitless disease.[36,37]

2

Where Do We Begin? Causes of Abnormal Brain Aging

RESEARCH IS BEING DONE in many arenas to discover the possible causes of dementia and Alzheimer's disease. While much is being done and even more is being proposed, there are few answers to this question. Many ask, "How can I prevent, or at least, dramatically reduce my risk of developing it?"

To answer these important questions, we must first understand when abnormal brain changes, dementia, and Alzheimer's disease begin. While no one can yet say for sure, there are some signs and symptoms that suggest that abnormal brain changes are occurring.

The development of dementia appears to follow a path that starts with mild, subjective cognitive impairment and moves to mild cognitive impairment and then to moderate to severe disease.

At onset, it appears that symptoms associated with "cognitive fluctuations" are among the earliest to develop in those more likely to develop dementia and Alzheimer's disease. Just prior to cognitive fluctuations, however, are changes that are called "subjective" in that most of the mental changes are not apparent to others, but may show up on the Mini-Mental Status Exam, or MMSE, even though these results are still considered normal. The MMSE is a simple test consisting of some basic questions and memory exercises given by many physicians in their offices to assess cognitive changes. Subjective changes could even be occurring in the general population up to fifteen years before problems are identified. Both the challenge and the opportunity with subjective symptoms are to identify these changes early enough to have an impact.[38]

Cognitive fluctuations, the next set of symptoms that may develop, comprise a set of symptoms that include staring off into space, experiencing daytime sleep of more than two hours, development of disorganized or illogical thoughts, and easily losing the train of thought. Individuals who report these symptoms may be in the earliest stages of the disease process.

While these things happen in healthy individuals, an increasing frequency of mental lapses is an early indication of dementia, according to some recent research. After assessing 500 individuals in a memory and aging study at the Washington University Alzheimer Disease Research Center, those with the symptom described as "cognitive fluctuation," or mental lapses, had 4.6 times the likelihood of development dementia.[39]

One of the best places to determine whether there is a problem with mental functioning is in a physician's office during the physical exam. It's a good opportunity to determine whether an older individual is experiencing cognitive fluctuation or other symptoms of abnormal brain aging.

Yet, diagnosing mild cognitive impairment can be difficult with few clinicians equipped to do so adequately. Few talk about what can be done to prevent the progression of mild cognitive impairment—or better yet—protect the aging brain from decline. We need to stop it in its tracks before it has time to do irreversible damage. Many barriers to diagnosis by primary care physicians exist, from lack of recognition of what the symptoms suggest and denial, to a belief that there is nothing that can be done to impede symptom progression. Family members may resist diagnosis out of fear of stigma, financial concerns, or lack of awareness of how to obtain help.[40]

It appears to be more difficult to identify Alzheimer's disease in those over eighty years of age, according to recent evidence, because the pattern of symptoms is not as distinct in those considered the "very old." Those defined as the "young old" by the study, those between the ages of sixty-one and seventy-five, showed greater brain changes when diagnosed with Alzheimer's disease than those who were much older, making detection and diagnosis in older age groups more challenging. What it means, then, is that the same approach to detection will not work for all age groups.[41]

Recent study has shown that early intervention in people with dementia could, in fact, be valuable based on the "plasticity" of the brain. The prevailing theory is that the brain can adapt to changing stimuli by recruiting neurons to develop new pathways to overcome limitations in brain function. This has been known to occur in cases of coma and paralysis.[42]

In a study of thirty subjects with mild cognitive impairment who were at high risk for developing Alzheimer's disease, improvement was noted when mental stimulation and cognitive training were done. This involved getting the subjects to read and respond repetitively to words and word patterns over a six-week period. Brain imaging with magnetic resonance imaging (MRI) before and after cognitive training showed that the

brains of these older subjects were able to adjust after the training and the changes in brain structure were measurable.[43]

What is Really Happening to the Brain?

Types of Dementia and Brain Changes

One of the biggest questions being asked related to brain aging and the development of dementia is, how can I recognize when brain changes are occurring? Research now suggests that many of these changes are evident as much as a decade before the most recognized symptoms of dementia are apparent. It's during these earliest stages that there is the greatest opportunity to intervene in the course of the disease with appropriate therapies.[44]

When we consider dementia, it is sobering to learn that there are over 100 different types, each with symptoms involving some degree of loss of mental, physical and behavioral functions that is progressive. Practically speaking, most discussion revolves around the four general types of dementia now recognized: Alzheimer's disease, vascular cognitive impairment, dementia with Lewy bodies, and frontotemporal dementia. Characteristically, memory loss accompanies each of these types of dementia. It is what happens in the early stages of this disease that makes dementia hard to recognize. It's also an area of intense research as scientists try to define the progression of dementia and

Alzheimer's disease in their earliest stages to make diagnosis and treatment easier through new types of imaging, cerebrospinal assessment, and biomarkers indicating brain changes.

It is only within the last ten-to-fifteen years that mild cognitive dementia has been recognized as a stage within the progression to Alzheimer's disease, though it is not always a harbinger of a worsening prognosis. Mild cognitive changes that are concerning include those that impair performance and function that would otherwise be appropriate for age and abilities. Often, the individual is unable to handle finances, cook, shop, or function socially. Someone with dementia may have trouble with word retrieval, retaining information and recognizing familiar cues in the environment. On the other hand, mild cognitive impairment not leading to dementia would not affect these types of function.

Other types of mental impairment occur and are known to accompany conditions such as normal pressure hydrocephalus, Parkinson's disease, and Creutzfeldt-Jakob disease.

Alzheimer's Disease

Alzheimer's disease is a progressive degenerative disorder attacking nerve cells in the brain. It is the most common form of dementia among older Americans, accounting for 60–70% of all cases in individuals under the age of seventy-one and 90%

of all cases under the age of ninety. It is characterized by the appearance of plaques and tangles in the brain, the physical changes that have been correlated with decreased memory, impaired thinking, and behavioral changes.

This disease was first described in 1906, when German physician Aloysius "Alois" Alzheimer first observed plaques and tangles in the brain of a fifty-year old woman who had died of an unusual mental illness. Since this initial observation, many studies have been conducted by researchers to identify underlying changes and genetic mutations that may cause the body to deposit these substances in the brain.

Alzheimer's disease, a condition that was once described as senile dementia, usually develops after the age of sixty-five. About one-in-every-ten people over the age of sixty-five is now believed to have this type of dementia. The most important risk factor appears to be age, with the number of people who have the disease doubling for every five years of age after the age of sixty-five.

It can present in people as young as thirty, though it is rare. When it occurs in young people, there is usually a higher genetic susceptibility to the disease and those with it show more of the brain changes—known as plaques and tangles—characteristic of the disease.

Recent studies show that, while symptoms may not occur in the vast majority of people as young

as thirty, the disease begins to develop then. Early intervention and risk management may be one of the important keys to stopping this disease.

When Alzheimer's disease occurs in older people, there are fewer of these brain changes, though they still are found in great numbers, suggesting that there may be a combination of environmental, lifestyle, and genetic factors that influence its development.

Three genes have been identified as risk factors for the development of Alzheimer's disease, all of which are dominantly inherited. The earliest gene to be identified is the gene coding for the lipoprotein known as apolipoprotein E or APOE, found on chromosome 19. This lipoprotein affects a specific lipoprotein in the body known as VLDL, or very low-density lipoprotein. We all have some amount of APOE because it helps transport cholesterol in the bloodstream to the liver, where it is used. There is a specific type of APOE, however, which is known as APOE e4, and only 15% of people actually have this type. APOE e4 substantially increases the risk of Alzheimer's disease in those who have the gene and decreases the age of onset. In contrast, those with the APOE e2 gene have a decreased risk of developing Alzheimer's disease.

While we don't completely understand why there is an increased risk with certain genetic alleles, it appears that family history and other

environmental influences play a role. The APOEe4 gene seems to be associated with an increased amount of amyloid beta plaque buildup in the brain of those with Alzheimer's disease and this plaque buildup is toxic to neurons.[45–47]

Through research, we've also learned that these genetic alleles increase the risk of an unfavorable response after head injury by as much as fourteen times in individuals with them when compared to individuals with other APOE genotypes. Head injury, traumatic brain injury, and concussion also appear to be risk factors for the development of dementia. In one collaborative study being conducted by the University of Washington and several veterans groups, evidence suggests that post-traumatic stress disorder may be a risk factor for developing dementia, as well.[48–52]

When these brain changes are found, they are often associated with nerve degeneration and decreased memory and cognition. In addition to being present in the brains of patients with Alzheimer's disease, plaque buildup has been found in patients with Mad Cow disease (Creutzfeldt-Jakob Disease), Parkinson's disease, Huntington's disease, brain injury, and in certain chronic infections like Lyme disease.[53]

What Are the Plaques and Tangles?

Plaque is found to build up in and around the brain cells of patients with Alzheimer's disease.

It is formed from a protein substance called amyloid beta. (Also known as Abeta, many studies also refer to it is beta-amyloid—it is all the same thing.) Before Abeta forms, however, a breakdown has to occur involving amyloid precursor protein (APP), a substance found normally in the membrane of brain cells. When abnormal processes occur, Abeta is formed from cleavage of APP rather than neuroprotective compounds. Neurofibrillary tangles are formed from another protein called tau and are found in highest number in the neurons of dying cells. Patients with Alzheimer's disease have these in higher numbers.

No one knows for sure how the plaques and tangles form, but they are believed to be part of the loss of memory and other symptoms associated with this and other diseases.[54,55]

The accumulating plaques and tangles are neurotoxic and the nerve cells break down and die more quickly than the body can repair them. Research now suggests that it is the earlier forms of the plaques and tangles that cause damage to cells, not the Abeta found in later stages of the disease process.[56]

When nerve cells die, information exchange at the synapses—the places where the neurons communicate with each other by exchanging information through neurotransmitters—begins to decline. Areas of the brain begin to atrophy and, in Alzheimer's disease, actually shrink.

Some researchers now suggest that the reason Abeta accumulates is to reduce cholesterol in the brain as a protective response.

Up until recently, dementia could only be diagnosed during autopsy following the patient's death. In recent years, however, brain scans with either magnetic resonance imaging (MRI) or positron-emission tomography (PET) are used to distinguish the type of dementia that a patient has long before the death of the patient.

In fact, these newer imaging techniques show Abeta formation in the brain ten years or more before symptoms of dementia develop. Evidence suggests that those with mild cognitive impairment who show a positive result for Abeta plaque through PET scanning have thirteen times the risk of development of Alzheimer's disease than those who do not show evidence of the protein. In a study tracking changes in Abeta plaque in those with mild cognitive impairment, results suggest that it is not this protein that causes dementia; but it creates inflammation and neurofibrillary tangles that damage neurons, especially in the temporal lobes, areas that are vital for memory.[57]

Research is focusing on identifying a simple biomarker that would indicate when brain changes are occurring. At least one biomarker has been identified as an early indicator for the development of Alzheimer's disease in those with mild

cognitive impairment. Scientists believe that this protein, known as soluble amyloid precursor protein beta, found in the cerebrospinal fluid of those with mental changes, may be a good indicator of developing dementia.[58,59]

Other Types of Dementia Affecting the Brain

Vascular Cognitive Impairment or Vascular Dementia

Vascular cognitive impairment, also known as vascular dementia, is the second leading cause of dementia in many countries, accounting for 15–30% of cases.[60] In some parts of Asia, it is the leading cause of dementia.[61]

This neurological disorder is caused by an array of conditions affecting vascular integrity.

People with vascular dementia will have a previous history of stroke, transient ischemic attacks, heart disease, high blood pressure, obesity, or diabetes. Another way of describing this type of dementia is "dementia due to cerebrovascular disease."[62]

Vascular dementia is caused by fatty deposits in the arteries that affect circulation to the brain, increasing the risk of strokes. Vascular damage and insult occurs, whether from stroke, white matter atrophy, or hemorrhage, that leads to brain cell death, cognitive impairment and, ultimately, functional impairment. It is similar to

Alzheimer's disease in that it manifests with cognitive and intellectual impairment. It can be so subtle in the beginning that it goes unnoticed. Difficulty with tasks of daily living does not show up until the condition is in the mid to late stages.[63]

Dementia with Lewy Bodies

At the time Alzheimer's disease was being described by the scientist, Alois Alzheimer, another scientist noticed some changes in brain cells of patients with Parkinson's disease, assessed after death. F. H. Lewy was the scientist who made this initial observation and others have studied these brain abnormalities in greater detail to understand how they contribute to dementia.

Lewy body dementia accounts for 12–20% of cases of dementia. A protein known as alpha-synuclein forms in the nerve cells of the brains of those affected. These proteins are also found in the brains of those with Alzheimer's and Parkinson's diseases, which are clinically similar. Dementia with Lewy bodies is also distinct in that there is severe nigrostriatal dopaminergic neurodegeneration not found in Alzheimer's disease.

Some research shows that neuroinflammation, particularly with the inflammatory cytokine known as interleukin-1, may be a factor in the development of Lewy body dementia, as well as other forms of dementia.[64,65]

In this type of dementia, there are problems with memory, visual hallucinations, muscle rigidity, tremors, fluctuating cognition, and visuospatial distortions. Awareness and attention varies, along with lethargy, and staring into space for long periods of time. The individual with this type of dementia may be excessively sleepy during the day and have rapid-eye movement (REM) disorder at night, during which they act out their dreams (something suppressed in those not affected by this disorder). Of all the forms of dementia, this one is most responsive to acetylcholinesterase inhibitors, though there is currently no FDA approved drug for it. Antipsychotic drugs should not be used in dementia with Lewy bodies since they make the hallucinations and behavioral problems worse.

Dopaminergic transporter SPECT imaging is a form of imaging that can be used to diagnose whether a patient has dementia with Lewy bodies or Parkinson's disease with concurrent dementia versus Alzheimer's disease. Results of this type of imaging are normal in those with Alzheimer's and abnormal if one of the other forms of dementia is present.[66]

Survival time after diagnosis is about eight years, similar to that of Alzheimer's disease and symptoms become progressively worse over time.

Frontotemporal Dementia

Frontotemporal dementia describes a group of disorders affecting the frontal and temporal lobes of the brain and accounts for about 10–15% of all cases. In contrast to Alzheimer's disease, which primarily affects individuals over the age of sixty-five, frontotemporal dementia most typically begins between the ages of forty–seventy. Tau protein accumulates in the brain and several types of mutations occur leading to brain atrophy. This form of dementia is characterized by changes in personality and marked loss of language skills.

There is no known treatment to prevent or retard the progression of frontotemporal dementia. Antidepressants and antipsychotics are commonly given to manage symptoms and personality changes. It is assessed through MRI or CT scans of the brain.[67]

In addition to these more common types of dementia, there are two additional conditions that are important to note.

Mild Cognitive Impairment

Mild cognitive impairment is a condition in which one has difficulty with language, memory or some diminishment of mental function, but not enough to interfere with activities of daily living. It is diagnosed primarily by eliminating other possible causes—therefore a diagnosis of exclusion—and

there is an increased risk of developing Alzheimer's disease. Factors that seem to increase the risk of mild cognitive impairment include a family history of Alzheimer's disease, depression, traumatic brain injury, metabolic disorders, ethnicity, and gender. Hispanic and African American individuals are at elevated risk for developing mild cognitive impairment and more women than men are at risk.[68]

Many clinicians consider mild cognitive impairment as the "prodrome" or beginning stages of Alzheimer's disease, so early detection and diagnosis is important in reducing risk of progression. According to studies, a diagnosis of mild cognitive impairment precedes Alzheimer's disease in 35% of those affected and begins at least five–six years before.[69,70]

It is this long pre-clinical phase that was noteworthy to researchers when they assessed the results of two long-term studies taking place over the course of sixteen years, the Religious Order Study and the Rush Memory and Aging Project. This data was especially surprising since science is aggressively trying to find ways to identify cognitive decline and arrest or slow it down. If memory changes occur years before mild cognitive changes can be detected, then it makes early identification more challenging. At the same time, those in the study who did not develop Alzheimer's disease did not demonstrate any cognitive changes.[71]

A very interesting gender difference was found in a recent study of mild cognitive impairment. Researchers found that about 16% of men have some degree of mild cognitive impairment without having dementia and these results were higher than those found in women. This gender difference suggests that women, who have a greater incidence of Alzheimer's disease overall, go from normal mental function to dementia when they are older and that this transition occurs more rapidly to outright dementia.

The frightening statistic reported by the researchers was that, if you take these results and add them to the numbers who already have some form of dementia or Alzheimer's disease in the population, it's clear that 25–30% of the population is already affected by some type of cognitive decline.[72,73]

Another population at risk for mild cognitive impairment is retired NFL players, according to a preliminary study of 633 former athletes presented at the Alzheimer's International Conference in 2011. According to researchers, up to a third of these players are at risk for dementia, a statistic that is far above the incidence in the general population. It's speculated that repetitive head injury or concussion may be an underlying cause, though other risk factors such as hypertension, obesity and diabetes were also present in many individuals in the study. Despite the increased risk, however, players with mild cognitive risk on testing

were all high functioning when assessed during the study.[74]

New evidence suggests that even mild cognitive impairment can significantly impact longevity and life expectancy. In a study of nearly 4,000 adults, cognitive impairment that ranged from mild to moderate in severity increased the odds of dying. Those who were considered to be of normal cognitive function survived an average of 129 months, while those with mild impairment survived 106 months, and moderate to severe survived sixty-three months during the study.

Life expectancy, then, may be affected by the degree to which one has developed cognitive impairment and may be something that will be monitored by physicians during regular physical exams, just like they monitor blood pressure, diabetes, and other chronic illnesses.[75]

In fact, loss of brain cells in the hippocampus of the brain may be a risk factor for dementia. A study of 142 individuals with varying levels of cognition compared development of dementia with the size of the brain and hippocampus. Volumes were measured via MRI at the beginning of the study and then a year and a half later.

As mentioned earlier, neurodegeneration tends to reduce overall brain volume, leading to significant atrophy of the brain. The risk of developing dementia and Alzheimer's disease increases when people lose large numbers of cells in the hippocampus.[76]

In an important study of hippocampal shrinkage, researchers found that by the time someone has mild cognitive impairment, there is already significant shrinkage of the hippocampus. If Alzheimer's disease is already diagnosed, then the loss of cells through the brain is extensive. If the patient was considered normal at the time the study began, but had a smaller hippocampal area of the brain and an increased rate of shrinkage, there was a two-to-four times increased risk of developing dementia when compared to those who were not experiencing rapid changes in brain volume.[77]

Within the clinical setting, it is still difficult to test patients for mild cognitive impairment. Screening tools identified to date are not easy to use. The Emory University School of Medicine is developing one possible solution to help identify mild cognitive impairment. The solution is the tool, DETECT, otherwise known as the Display Enhanced Testing for Cognitive Impairment and Traumatic Brain Injury tool, which may be an important step in finding a prescreening method for early brain changes.[78]

With the advent of imaging techniques identifying degrees of neurodegenerative changes, rating scales have been proposed describing the pathologic stages that occur with decline in mild cognitive impairment, often considered to be preclinical Alzheimer's disease.

Recently guidelines for the neuropathologic assessment of Alzheimer's disease were created by a consensus panel of experts from the US and Europe.[79–82] The following summarizes the basic steps toward dementia commonly observed in patients.

Stage 1:

During this stage, imaging identifies amyloid beta deposition in the brain through either cerebrospinal fluid analysis or PET scan. The patient is not, however, experiencing any cognitive decline.

Stage 2:

In this stage, the patient not only shows evidence of abnormal brain changes through assessment of biomarkers found in the CSF, but there is now an apparent change in the size of specific areas of the brain signifying brain atrophy. Cognition may still be normal at this time.

Stage 3:

In this stage, neurodegenerative changes are accompanied by some mild cognitive impairment.

Eventually, biomarkers may take over as the diagnostic standard for assessment of Alzheimer's disease, replacing pathologic interpretations.

Normal Pressure Hydrocephalus (NPH)

Normal pressure hydrocephalus (NPH) is often misdiagnosed as Alzheimer's disease or dementia. Because of this confusion, it can often take seven to nine years to identify patients with this condition, which is treatable and usually reversible once diagnosed. Most individuals with normal pressure hydrocephalus are over sixty-years of age. It may occur after brain injury, stroke, and meningitis or in response to a brain tumor.

NPH is an abnormal increase in cerebrospinal fluid caused by blockage of normal flow, leading to symptoms that include abnormal gait, urinary incontinence and dementia. Patients have a shuffling gait not unlike that of Parkinson's disease, but do not have any significant tremor or rigidity. It does not respond to levodopa/carbidopa therapy.[83]

3

What You Don't Know Can Lead to a Big Problem Later On: Understanding the Symptoms of Dementia and Alzheimer's Disease

THERE IS NO ONE way that symptoms show up in someone developing age-related dementia or Alzheimer's disease. While we all experience a little of this from time to time, the indication that there is a problem would be how often memory problems occur and if they are they getting worse over time.

Signs of brain aging include difficulty remembering names, directions, words, appointments; disorientation, memory lapses, depression, and anxiety, enough to affect the activities of daily

living. These early problems signal the beginning of a breakdown in brain circulation and nerve communication.

It is early-onset Alzheimer's disease, or disease that begins before age sixty, which poses a diagnostic challenge, however, in that memory changes may not be among the first symptoms to appear. Many early-onset changes are atypical and may affect vision, behavior, or language. When cognitive changes are the first sign of disease, then diagnosis is usually accurate, but it is often misdiagnosed when other symptoms present first.[84,85]

Those who are progressing toward cognitive impairment and dementia may exhibit many of these commonly observed symptoms:

1. Difficulty learning and retaining new information that affects daily activities
2. Forgetting recent events and appointments and misplacing objects
3. Difficulty handling complex tasks, like balancing a checkbook or planning an event
4. Not knowing what to do when problems come up and exercising poor judgment
5. Disorientation to time and place, such as getting lost in familiar places
6. Increasing difficulty in finding the right words to say
7. Challenges in understanding and responding to what is seen or heard

8. Acting more irritable or suspicious than usual
9. Increasing apathy and withdrawal from conversations or activities
10. Mood and personality changes

These symptoms often occur with each of the types of dementia described earlier, including Alzheimer's disease. The degree to which they occur indicates whether symptoms are mild, moderate, or severe.

Warning signs of mild to moderate dementia that would impair driving include difficulty parking within defined spaces, not noticing traffic signs, confusing the gas and brake pedals, and stopping in traffic for no apparent reason. When considering whether someone should be restricted in their ability to drive, look for patterns and incidents that might justify action. At the same time, families may be observing some of the other memory patterns described above.[86]

While memory loss is characteristic of both dementia and Alzheimer's disease, there are differences in onset and severity. With Alzheimer's disease, memory loss includes forgetting recently learned information and difficulty performing simple and familiar tasks. Loss of financial skills that one once possessed is also an early sign of Alzheimer's disease.

Problems with language may go beyond forgetting words occasionally and include problems

with making substitutions for simple words. For example, a cup may become "that thing that holds water or coffee." As dementia progresses, there may be difficulty communicating through language altogether.

A condition that is frequently described as "motion blindness" is a big reason that some Alzheimer's patients lose their way and become disoriented. It can simply be described as an inability to judge whether they or their surroundings are moving.

The part of the brain that interprets motion is affected and the patient literally cannot see where they are going, according to a recent study. Those affected become blind to the information that gives them feedback on where they are going. It is as if they were walking around with closed eyes. It becomes a disorder of "perception as well as memory," according to Dr. Duffy, the lead researcher.[87–89]

Others have described a type of unexplained loss of vision that affects the ability to read and write as a "visual variant" of Alzheimer's disease. In this condition, which is relatively rare, individuals have trouble reading, often cannot read their own handwriting, and have difficulty writing. Examination of these patients using the Mini-Mental-Status Exam (MMSE), a common test used to identify cognitive changes, shows scores consistent with those who have Alzheimer's disease.[90]

In fact, the association with poor vision may be more extensive than previously believed. In people who develop dementia—particularly Alzheimer's disease—late in life, the evidence suggests that their vision is poorer and that they have not had vision assessed very often prior to becoming diagnosed with the disease. Those with normal cognitive function had better vision and had received more ophthalmologic assessment during their lifetime.

Could it be that under-treatment of visual problems leads to cognitive decline? In a study of 625 patients with normal cognition prior to the study, those who maintained better vision and had more follow-up care over the course of the 8.5 years of the study had a 63% reduced risk of developing dementia. It is likely that one of the first set of symptoms that occurs with the onset of dementia is visual problems, which affects the ability to orient spatially, perceive colors, and orient to what is occurring in one's surroundings. Other disorders, including that of macular degeneration, may further affect visual acuity. These may be predictive of cognitive decline, not a result of it.[91]

Research has also identified nutritional and vitamin deficiencies that cause lesions in the eye and are perhaps related to the development of dementia.

Alzheimer's disease often unfolds over the course of seven–ten years, though abnormal brain changes have been occurring for much longer.

A typical scenario may breakdown as follows:

1. Initially, the individual is unimpaired and there is no dementia present.
2. Over the course of two to five years, very mild cognitive decline may occur, progressing to mild cognitive impairment. When mild impairment is obvious, neurodegenerative changes are usually extreme.
3. Mild cognitive impairment progresses over time to mild cognitive decline.
4. Progression to moderate cognitive decline takes another two–four years, during which time memory becomes more significantly impaired and there is a loss of the ability to function independently or at home.
5. There begins a progression toward moderately severe cognitive decline to severe cognitive decline and finally, very severe cognitive decline.

Assessment and Diagnostic Recommendations for Alzheimer's and Dementia

If Alzheimer's disease or other forms of dementia are suspected, it's important to get a good assessment and establish a connection with a doctor who can help you manage the illness and implement strategies for reducing risk. Assessment involves four distinct objectives. The first

is to assess whether dementia is actually present. Next, are the symptoms consistent with a diagnosis of Alzheimer's disease? The next step in the assessment of any dementia type illness is to be sure that there are no alternative diagnoses possible. Lastly, if dementia is indeed present, are there aspects of the disease process that could benefit from treatment?[92]

When considering any diagnosis of dementia, it is important to make sure that there are no physical causes for symptoms, such as brain lesions, subdural hematoma, thyroid disease, vitamin deficiencies, or chronic infections. While the progression of cognitive illnesses generally rules out other causes, they can still be present.

If you are the patient being assessed, you will be asked questions about your general health, past medical problems, and the ability to carry out the activities of daily living. Part of any comprehensive assessment will be medical tests, including fasting blood tests, urine testing (especially hormone evaluation), and spinal fluid testing. Sometimes imaging is ordered, including brain scans and other types of tests to rule out physical causes.

Most assessments involve a series of tests to measure decline in memory, assess problem-solving abilities, attention span, ability to count (loss of financial skills is an early indicator of mental decline), and language. Tests commonly used

include the Mini-Mental Status Exam (MMSE) and the Alzheimer's disease Assessment Scale (ADAS).

The MMSE asks the patient questions requiring recall, speech, attention, orientation, and language use and takes only a few minutes, so can be administered in a doctor's office. Scoring is on a numeric scale, ranging from one-to-thirty. The lower the score is, the greater the cognitive impairment, with anything less than 24 being associated with some form of dementia.

The ADAS—Cognitive sub-scale (ADAS-Cog)—is a test that checks for the ability to remember and respond to spoken cues, similar to the MMSE, which takes about thirty minutes to administer. Scores on this test range from 0 to 70, with higher scores associated with increasing cognitive impairment.[93,94]

Another brief test that can be done in a doctor's office is the clock drawing task known by the creative term, CLOX. The patient is asked to draw a clock face along with the numbers and clock hands. Then, the patient is asked to show a specific time on the clock, usually something on the quarter hour, such as one forty-five (1:45) or two fifteen (2:15). Impairment is measured by the degree of difficulty one has with performing this task.[95]

The clock drawing test is often combined with the evaluation tool known as the Mini-Cog Assessment Instrument that involves three words that the patient is asked to recall. It takes about three

minutes to do and no equipment is required, and responses seem to be independent of education or language. The patient is first asked to remember and repeat three words. Then, the clock drawing test is given, followed by a request to the patient to repeat the three words they were previously asked to remember. If no words are recalled, the patient is given a score of 0, which is a positive test for dementia. If the patient is able to remember one or two words but has a poor clock drawing test, then it is positive for dementia. If the patient recalls one, two, or three words and has a good clock drawing test, then it is negative for dementia.[96]

The Late-Life Dementia Risk Index is another tool that is based on a 15-point assessment scale. It's designed to stratify older adults into dementia risk categories of mild, moderate, or high risk of development within the next six years. The goal is to identify patients early so that prevention and treatment can begin before symptoms are significant. In a study involving 3,375 patients in the Cardiovascular Health Cognition Study, this tool accurately predicted the progression to dementia within six years. Those patients with low scores had only 5% risk, while those with higher points had a risk of 50%.[97]

If dementia is suspected following assessment, then attention will be given to activities of daily living and the ability to provide care, including

daily function, degree of impairment in cognition, coexisting medical conditions, any present disorders of mood and emotion, and caregiver status—is there one now or is one needed?

A strong predictor of future development of Alzheimer's is the inability to identify ten odors: clove, leather, lemon, lilac, menthol, natural gas, pineapple, smoke, soap, and strawberries.

Another new test that shows promise in the identification of mild cognitive impairment in those at risk is known as the Display Enhanced Testing for Cognitive Impairment and Traumatic Brain Injury tool (DETECT). It's hoped that a method like this can be used in physicians' offices to standardize and improve the identification of early cognitive changes. When tested against controls, this test appeared to be able to differentiate those elders with mild cognitive impairment.[98]

While there are methods available now to identify dementia and Alzheimer's disease, the limitation on the part of both the patient and his or her family is often recognizing that cognitive changes are indeed occurring and accepting the diagnosis.

Brain Assessment Techniques

Up until recently, the only way to diagnose the brain changes that occur with Alzheimer's disease was through autopsy after death. When symptoms of mental decline were detected in patients, often the diagnosis was made by excluding all possible other

causes and this method was not infallible. It often missed some of the other causes related to mental changes described above and delayed the provision of necessary medical care to those affected.

Thankfully, assessment techniques have improved substantially, though a detailed clinical history and neurological exam are still a very important part of the process. Neurological imaging has now evolved in ways that are very helpful in making a more accurate diagnosis and research is identifying important biomarkers indicating earlier and earlier stages of disease progression. Many studies are underway to identify these biomarkers.[99,100]

Assessment for dementia now includes many imaging techniques, such as ultrasound, magnetic resonance imaging (MRI), computerized tomography (CT), and positron emission tomography (PET) scans. In most cases, the individual undergoing assessment is given some type of contrast media that helps identify structures in the brain and then scanned to see what the activity is in specific areas known to be important for diagnosing neurodegeneration.

SPECT scans are a form of PET scanning that is being done in many centers around the country that can identify areas of deterioration in brain function early enough for those affected to modify some of their risk factors. Some long-term studies using SPECT functional neuroimaging

have been able to predict progression from mild cognitive dysfunction to Alzheimer's disease 93% of the time. Similarly, they were able to determine that the patient did not have Alzheimer's disease 81% of the time using this technology.[101]

In the assessment of abnormal brain aging, it is crucial to find ways to study time of progression from mild cognitive impairment to full Alzheimer's disease so that there is time to begin therapies that may slow the disease. The goal is to find out what is happening in the brain before symptoms become apparent, because symptoms usually mean that neurodegenerative changes have progressed to a point there is little opportunity to reverse them.

Studies are underway looking at cerebrospinal fluid markers indicating that amyloid beta levels are elevated in the brain. PET imaging is a way to determine whether a specific area of the brain—the hippocampus—is decreasing in size, or atrophying, suggesting decreases in cognitive function. The degree to which this atrophy has occurred gives doctors an indication how far along the patient is in progression toward dementia and Alzheimer's disease. Many now believe that the presence of the amyloid beta deposits in the brain is just a harbinger of changes in brain pathology but not the actual cause of memory loss.[102]

Proton magnetic resonance spectroscopy is a very new method that can identify early brain

changes in individuals without symptoms and is a noninvasive method of assessment.[103]

Cerebrospinal fluid (CSF) assessment may reveal those at risk for Alzheimer's disease[104] as early as 10 years before diagnosis. When CSF testing was conducted in 137 patients with mild cognitive impairment, results showed reduced levels of beta amyloid and increased levels of total tau protein, two markers found in association with progression to Alzheimer's disease. When these results were found with CSF assessment, they were found in 90% of those who developed Alzheimer's disease at a later date. On the other hand, those with normal levels of these proteins in CSF fluid did not progress toward the disease. Based on their results, researchers speculated that beta amyloid is an early marker of dementia risk, whereas tau protein is a later sign indicating worsening pathology and degeneration of neurons.[105]

4

What Increases Your Risk of Abnormal Brain Aging?

MANY THEORIES EXIST ABOUT the process of abnormal brain aging. While there are mechanisms that we may not be able to counteract, many of them can be prevented or addressed before irreversible damage is done. For the most part, dementia is something that occurs late in life, which means that efforts focused on delaying symptoms may be almost as effective as a "cure" and could reduce the onset of the disease significantly.

Among the causes being studied are chronic inflammation, oxidative and nitrosylative stresses, high cholesterol, mitochondrial damage, and many

more. These processes are thought to initiate and promote neurodegenerative changes. There is significant overlap between possible causes. Impaired blood sugar metabolism, for example, can affect blood pressure and create oxidative stress and elevate inflammation in the body. Mitochondrial dysfunction can affect one's ability to exercise, contributing to obesity, inflammation, and altered insulin-signaling pathways.[106]

The possible causes of brain changes leading to dementia and Alzheimer's disease are complex and the numerous causes that have been hypothesized are summarized below. Before beginning any supplement or dietary regimen, however, it is a good idea to consult with a physician who is knowledgeable and aware of natural medicine and dietary supplementation for best effect in the treatment of any disease.

Chronic Inflammation

Inflammation is a word used to describe many causes of disease, from hypertension and cardiovascular disease to insulin resistance and diabetes. It is an underlying factor in many illnesses, but each condition develops in different ways, leading to confusion and difficulty in knowing what to do and when to do it to improve health.

In the study of Alzheimer's disease and dementia, many studies suggest that damage to blood

vessels and circulation is an underlying cause in their development. Though these are neurodegenerative illnesses, researchers associate them with a state of chronic inflammation and oxidative stress in the body. This inflammation, in turn, causes abnormal brain aging. Chronic inflammation has been shown in many studies to be a factor in the development of dementia because it destroys brain cells.[107]

High blood pressure, insulin resistance, and diabetes are several of the results of inflammatory and oxidative damage to the body. These conditions are the result of systemic vascular damage and blood sugar changes, causing an imbalance in the body's ability to function.

Hypertension

The Finnish Cardiovascular Risk Factors, Aging, and Dementia Study put a lot of the risk factors related to the heart into perspective. Participants were evaluated over the course of five years for factors ranging from body mass index to smoking status and lipid (cholesterol) levels. At the last exam, they were assessed for dementia using a three-stage test.

Results showed that high blood pressure increases the risk of dementia, especially among those who have an elevated systolic blood pressure at midlife. Those individuals with a systolic blood

pressure over 140 mm Hg have the highest risk, followed by moderate risk in those with a systolic blood pressure of 120–139 mm Hg. The lowest risk for dementia occurs in those with systolic blood pressure measurements under 120 mm Hg.[108,109]

The systolic blood pressure measurement indicates the pressure of heart contractions and, if allowed to elevate over time, increases damage to the vascular system. These degenerative processes begin early, increasing risk of dementia in those who have long-term elevated blood pressure. The point to be understood here is that blood pressure management should begin early enough to make changes before midlife.[110,111]

When circulatory deficits are allowed to continue unchecked, they increase the risk of cardiovascular and endocrine dysfunction. It generates a pro-inflammatory cycle in the body that can affect the protective mechanism found in the blood brain barrier.

Frail seniors, the group most likely to show symptoms of dementia and Alzheimer's disease, are more likely to have inflammatory processes occurring in the body. Frailty is linked to Alzheimer's disease, and this becomes a circuitous pathway. The key is to reduce inflammation in the body, a process not always as easy as it seems to do.

Brain microbleeds may be one of the ways that vascular damage contributes to the risk of

dementia and Alzheimer's disease. Some evidence suggests that blood vessel damage and the deposition of amyloid in the brain may act together to create neurodegenerative pathology.

Despite the research, there is not a clear association yet. The best recommendation is to continue to reduce these risk factors, which improves overall health and which may help reduce the likelihood of development associated brain changes.

Insulin Resistance and Diabetes

Many have speculated that insulin resistance, characterized by increased abdominal girth, elevated blood pressure, and blood sugar dysregulation, is a factor in the development of Alzheimer's disease. Some have even called insulin resistance the "third type of diabetes" because of its possible association with dementia. When fasting blood sugar levels are measured in the blood, those with insulin resistance will have blood sugar levels above the normal range but below the level for frank diabetes. This gray area, reflecting problems with blood sugar management, offers both hazard to the body and opportunity for improvement if it can be controlled.[112]

There is an emerging body of information that suggests that insulin abnormalities and insulin resistance may contribute to the formation of amyloid beta precursor protein and Abeta. Insulin

is essential for energy metabolism in the periphery and there are many insulin receptors in the brain, especially in areas that support memory and recall. Insulin regulates metabolism of the beta-amyloid precursor protein and tau, both building blocks of amyloid plaque and tangles. It may also increase the intracellular effects of Abeta and interfere with its degradation in the brain.

Recent research seems to support the belief that insulin resistance can contribute to abnormal brain aging, with related health risks that include the development of type 2 diabetes, heart disease, obesity and increased cholesterol levels.

To examine this in greater detail, researchers looked at the HIGH diet (high saturated fat and high glycemic index foods) and the LOW diet (low saturated fat and low glycemic index foods) in individuals with mild cognitive impairment and those who were considered healthy. Glycemic index refers to the degree to which the food causes an insulin response in the body; high glycemic index foods have a high response from insulin and low glycemic index foods generate a low insulin response.

What they found was that consuming a diet high in simple, refined carbohydrates and high in the wrong kinds of fats, such as saturated fats, may increase the pathology that causes Alzheimer's disease. A diet that was comprised of complex carbohydrates and low in simple carbohydrates,

along with being low in saturated fat, seemed to confer better protection against the development of dementia.[113] These are all recommendations consistent with controlling insulin resistance and diabetes, as well.

In a three-city study of metabolic syndrome and the development of cognitive impairment in a group of French elders, metabolic syndrome contributed to overall decline in cognitive skills and in specific cognitive abilities in particular.[114]

Poorly controlled glucose levels can affect the health of neurons, leading to their loss over time and increase the risk of mild cognitive impairment. Other blood sugar risk factors for mild cognitive impairment include developing diabetes before turning age sixty-five, having diabetes for ten years or more, being insulin dependent, or developing complications for diabetes.[115]

Once insulin resistance and sugar dysregulation progress to the point of type II diabetes, there is increased risk of cognitive dysfunction and dementia, possibly from loss of neurons over time. It may also contribute to microvascular insult and brain atrophy. Those patients who showed diabetic retinopathy, an eye disease common in those with diabetes, were twice as likely to develop mild cognitive impairment.[116] In those with diabetes and Alzheimer's disease, a combination of diabetic medications and insulin was shown to reduce neuritic plaque density in the brain.[117]

Solutions:

- Reduce inflammation in the body by reducing risk factors.
- Maintain a healthy, controlled blood pressure.
- Maintain a healthy blood sugar by eating a diet of low glycemic index foods that are low in saturated fats and simple carbohydrates and containing complex carbohydrates.
- Treat insulin resistance to prevent mild cognitive impairment.
- Treat type II diabetes with a combination of insulin and other diabetic medications.

Oxidative Stress

Oxygen is an essential element in the body, powering many metabolic reactions and providing energy to cells. It is also a potential hazard in the body in that these processes produce free radicals, or singlet oxygen molecules, that can cause damage if they are not taken up by antioxidants that neutralize them. Oxidative stress, the term for this kind of tissue damage, may occur if the body does not contain enough antioxidants to reduce their impact on the body. Iron is another element that is prone to producing free radicals in the body.

In neurodegenerative diseases, such as Parkinson's, Alzheimer's, and amyotrophic lateral sclerosis, the brain may develop oxidative damage as a result of increased free radical production. These free radicals,

in turn, cause pro-inflammatory changes that increase pathology. Fortunately, the body has many antioxidant defenses in the brain and elsewhere, including mitochondrial-manganese containing superoxide dismutase and reduced glutathione.

It is believed that natural antioxidants, such as vitamin E (tocopherols) and carotenoids, cross the blood brain barrier to reduce oxidative stress and much research is occurring to identify dietary antioxidants to reduce their development and progression.[118–121]

Solutions:

- Take the antixoxidants, vitamin C, vitamin E, and others.
- Vitamin E is a fat-soluble antioxidant that may alter progression to Alzheimer's disease. Eat vitamin E rich foods, such as whole grains, eggs, milk, nuts, seeds, avocado, spinach, and unsaturated vegetable oils.
- Maintain an adequate intake of omega-3 fatty acids, particularly DHA.

Chronic Stress and Risk for Cognitive Impairment and Alzheimer's Disease

When we are under stress for a short amount of time, hormones are secreted by our adrenal glands to help us cope and often improve our performance. As stress becomes chronic, however, the adrenal

glands produce excessive cortisol that affects memory and function. It can lead to neuronal damage from the excessive production of cortisol in response to stress.

Chronic stress can have a significant impact on cardiovascular and digestive health, as well as impact our performance, memory, and mood. Chronic stress is considered to be a risk factor for the development of Alzheimer's disease by causing accumulation of beta-amyloid in the brain. In a recent study involving rodents, the ability to learn and remember was significantly impaired when levels of beta-amyloid were elevated in the presence of chronic stress.[122]

In a study of the effects of stress on the deposition of tau-protein in the hippocampus, researchers found a possible mechanism for its pathologic deposition in a population of mice. The stress compound, corticotropin-releasing factor, appeared to be altered when animals were repeatedly stressed, leading to increased deposition of tau-protein. Animals without the ability to respond to the stress did not develop higher levels of tau-protein, suggesting a possible relationship between stress levels and the development of cognitive impairment.[123]

Solution:

- Find ways to reduce stress and its impact on cardiovascular, cognitive and digestive health.

Glycation

Glycation is a pro-inflammatory process that occurs when foods are cooked at high temperature. Eating these foods contributes to the production of inflammatory cytokines, or compounds that promote inflammation in the body. As discussed earlier, inflammation is a major risk factor for the development of dementia.

When foods are cooked at high temperature, such as through broiling, grilling, and frying, the protein molecules in the foods are bound to glucose molecules, damaging the proteins. This process leads to the formation of advanced glycation end products (AGEs). AGEs accumulate slowly in the body until they become a significant factor in the development of chronic and age-related diseases. It's believed that many age-related diseases, such as arterial stiffening, cataract formation, and neurological impairment, may be partly due to the glycotoxins produced from cooking foods at high temperature. As damaged and degraded proteins accumulate, they cause cells to emit signals that induce the production of inflammatory cytokines.[124]

A Proceedings of the National Academy of Sciences study shows that consuming foods high in glycotoxins might cause a steady, low-grade state of chronic inflammation. When foods are cooked at high temperature, they also increase the formation of these glycotoxins in our tissues. It is

a sobering revelation that some of our modern behaviors may be quite toxic for us.

Similar to the discussion about insulin resistance and diabetes, the consumption of low glycemic index foods helps reduce insulin levels after eating and reduces the development of chronic inflammation. The modern American diet also includes foods high in arachidonic acid, the omega-6 fatty acid commonly found in increased amounts in foods like egg yolks, dairy products and beef, which can increase inflammatory reactions in the body. A high intake of these foods can lead to the production of inflammatory cytokines that increase inflammation in the body, leading to metabolic disorders that may be significant factors in the development of dementia and other neurodegenerative diseases.

L-carnosine is a di-peptide, a molecule formed from the combination of two amino acids. This compound can help reduce AGEs by binding to and deactivating these inflammatory molecules. Once this has occurred, macrophages are better able to eliminate AGEs from the body.

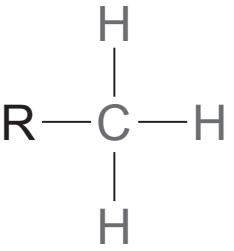
Solutions:

- Avoiding cooking foods at high temperatures. Boiling and poaching are the safest forms of cooking.
- Take L-carnosine daily to help reduce the degenerative changes induced by glycation

reactions. You should not take more than 600 mg of L-carnosine daily since it can cause muscle twitching in high doses.

Methylation Deficit

Methylation is a process in which the body turns one metabolic compound into another. The process involves a carbon with three hydrogen items attached to it, also known as a methyl group, which is then added to another compound to form a different substance in the body.



An example of a methyl group

Methylation involves the compound, SAMe, or S-adenosine methionine, which gives a methyl group to another compound, and this, in turn, creates homocysteine from SAMe. The vitamins B_{12}, B_6, and folic acid are necessary cofactors for this process to occur.

Homocysteine

When levels of homocysteine are high, it may irritate the blood vessels and contribute to increased risk of cardiovascular disease, stroke, and peripheral vascular disease. Studies also suggest that high blood levels of homocysteine may increase the risk of developing Alzheimer's disease. When plasma levels were detected in patients in one study in amounts greater than 14 μmol/L, the risk of Alzheimer's disease doubled. According to the authors of this study, "an increased plasma homocysteine level is a strong independent risk factor for the development of Alzheimer's disease."[125,126]

It's possible that half of the population may contain a genetic variation—a genetic polymorphism—that may increase the risk of dementia by inhibiting the absorption of folic acid. When a bioactive form of folic acid is used, known as methylfolate (also referred to as 5-MTHF), it crosses the blood brain barrier and is seven times more available to the body, reducing homocysteine levels and risk.[127,128]

Brain atrophy is a condition that occurs in the elderly, even in those with intact cognitive abilities. Brain atrophy proceeds much more rapidly, however, in those who are cognitively impaired. Researchers have looked for anything that might influence these brain changes and for ways to retard their progression.

Raised levels of homocysteine have been associated with brain shrinkage. In a study of high-dose B vitamins, including vitamin B_{12}, B_6, and folic acid, it was demonstrated that they can slow the rate of brain atrophy in those who are experiencing mild cognitive impairment. These vitamins reduced the level of homocysteine in the body when compared to those not taking them and reduced the rate at which the brain was shrinking. While researchers do not know if this has an impact on dementia, the study did show that those who had the highest levels of homocysteine in the group not taking the supplements did decline on test scores and those taking the supplements did not show test score decline.[129]

Vitamin B_{12} Deficiency

Vitamin B_{12} is important for synthesis of nucleic acids and results in megaloblastic anemia when it is deficient. If the ability to absorb vitamin B_{12} is compromised in the intestines by the loss of intrinsic factor, pernicious anemia results. It is a diagnosis that can easily be missed in the elderly and in those with compromised nutrient absorption.

Evidence has associated low levels of vitamin B_{12} and folate with a two-fold increase in risk of memory loss and Alzheimer's disease and other types of dementia that resemble Alzheimer's disease.[130–132]

Vitamin B_{12} taken with folic acid can help. One trial showed that taking 2 mg of folic acid plus 1 mg of vitamin B_{12} every day for twelve weeks could significantly lower serum homocysteine levels.[133]

Solution:

- Take methylfolate (natural, active folic acid) with B_{12} and B_6 for best effect.

Mitochondrial Dysfunction

With the exception of red blood cells, all other cells in the body contain about 2500 mitochondria per cell. These cellular components are commonly referred to as the powerhouse of the cell because they produce ATP, a vital source of energy for cellular metabolism. It's important for nutrient absorption, repair of cells, and elimination of toxins.

The electron transport chain is the energy factory that is found within the mitochondria and is the place where energy conversion occurs. As a result of its processes, many dependent on the use of oxygen, free radicals are created that have the potential to cause oxidative damage to the cell if they are not prevented from doing so.

Some evidence suggests that mitochondrial dysfunction leading to energy depletion is a factor in the development of Alzheimer's disease, Parkinson's disease, Huntington's disease and amyotrophic lateral sclerosis (ALS). The neurodegenerative changes that are stimulated when mitochondrial damage

occurs may be responsible for conditions associated with Alzheimer's disease, including impaired glucose use, increased free radical production, and increased oxidative damage. Mitochondria are passed down through the mother to her offspring and the observation that there is increased risk of development of Alzheimer's disease in the children of mothers with Alzheimer's disease suggests a possible connection to mitochondrial effects.[134]

Studies have also associated amyloid-beta found in the brains of those with Alzheimer's disease with its ability to induce mitochondrial dysfunction. In an animal study of mitochondrial dysfunction and Alzheimer's disease development, results showed that mitochondrial changes occurred even before any plaque deposition was found in the mice most susceptible to it.

A good strategy for prevention of Alzheimer's disease and other forms of dementia may be to support mitochondrial function through the use of things that support it, including supplementation with antioxidants and the hormones, estrogen and progesterone, which help support enzymatic response and suppress oxidative stress.[135,136]

Solutions:

- Support mitochondrial deficit by reducing oxidative stress.
- Supplement with CoQ10—supports the mitochondria from decay.

- Supplement with R-lipoic Acid.
- Supplement with Acetyl L carnitine.
- Supplement with B_{12}/folate.
- Supplement with NADH.
- Consider hormone replacement therapy.

Increased Risk with Lower Hormone Levels that Naturally Occur with Aging

In women, the primary sex hormones are estrogen and progesterone and in men, DHEA and testosterone. All sex hormones are found in both men and women, however, but in very different levels and these levels account for sexual differentiation.

Hormone changes occur in both men and women as they age. Age-related decline in growth hormone and its metabolites, and the anabolic hormones DHEA and testosterone, may be predictors of early mortality in some individuals. When multiple hormone deficiencies occur, they may be biomarkers for elevated risk.[137]

Hormone therapy may reduce risk and offer protection for age-related decline.[138] In observational studies, women who were receiving hormone therapy performed better on verbal and visual memory tests when compared to those who had never been treated. Interestingly, those women taking hormones had a different pattern of brain activity, showing increases in blood flow to the

hippocampus, an area of the brain often associated with age-related declines in function.[139]

In the Women's Health Initiative Memory Study, part of the Women's Health Initiative, women who received hormone replacement therapy before they reached the age of sixty-five appeared to reduce their risk of dementia more than women who did not receive hormone therapy. Risk of developing Alzheimer's disease or dementia was reduced by close to 50% in those using hormone replacement therapy at any age before sixty-five. If hormone therapy was begun after age sixty-five, it appeared to increase risk of dementia. Researchers suggest additional studies are needed to determine how hormone therapy reduces risk more specifically and urge that results be applied with caution.[140]

In the body, testosterone is comprised of both free testosterone and testosterone bound to sex hormone binding hormone (SHBH). The free testosterone is available to the body to a greater degree than the bound testosterone and may play a role in preventing Alzheimer's disease, In a study of 574 men between the ages of thirty-two and eighty-seven, testosterone levels were measured over a period of nineteen years. Both free and total testosterone levels were measured. During the study, fifty-four men developed Alzheimer's disease. While all men experience a drop in testosterone levels as they age, testosterone levels

dropped the most in the men who had developed dementia. Researchers have speculated that testosterone may prevent the buildup of beta amyloid plaque in the brain, which is associated with Alzheimer's disease.[141]

Improvement of Brain Injury with Progesterone

Evidence suggests females recover more quickly from brain injury than males do and the difference may be due to the increased levels of progesterone, which may have neuroprotective benefits. In studies conducted by neuroscientists, evidence suggests that progesterone helps the brain repair itself in a way that is similar to that which occurs during early development of the nervous system. Studies have shown that administration of progesterone improves outcome and overall survival when used in patients with brain injury. In one clinical study of 100 patients, the death rate was reduced more than 60% when progesterone was used.[142–144]

Solutions:

- Hormone replacement therapy for women before age sixty-five
- Hormone replacement therapy for men when testosterone levels are low

Vitamin and Mineral Deficiencies

Vitamin A

Vitamin A is an important fat-soluble vitamin that we obtain in two ways. The first way is through consuming animal products, such as dairy, liver and kidneys, and eggs, which contain vitamin A in the form of retinoids. The second way is through eating vegetables, especially carrots, which contain carotenoids, the plant-derived form of vitamin A. This vitamin is needed for normal growth and development and, when insufficient in the diet, can lead to blindness, especially night blindness, skin infections, and respiratory problems. The retinoids may, in fact, play an important role in the development of the brain from birth and the plasticity of the adult brain.[145]

Low levels of vitamin A may be a factor in the development of cognitive decline. Research has found that low levels of retinoic acid, the last step in the formation of vitamin A, may be a factor in the development of late-onset Alzheimer's disease. Studies are now looking for ways to test retinoic acid receptors and retinoic acid enzymes because of their possible role in preventing or reducing amyloid plaque formation.[146]

Solution:

- Maintain an adequate intake of vitamin A from plant and animal sources.

Vitamin D

Vitamin D is one of the fat-soluble vitamins, along with vitamins A, E, and K. Vitamin D is absorbed through the skin when we are exposed to the sun and obtained through the diet and dietary supplements. Foods rich in vitamin D are the cold-water fatty fish, like cod, and vitamin D-fortified products, like milk, cereal, and orange juice.

Because of inadequate sun exposure and dietary intake, many people are either deficient or insufficient in their intake of vitamin D. In addition to supporting bone health, vitamin D seems to have an impact on the central nervous system (CNS), acting much like a neurosteroid. When intake is adequate, vitamin D appears to be neuroprotective as well as anti-inflammatory.

While vitamin D does appear to cross the blood brain barrier and go into the brain, no one knows yet what functions it might have there. Low vitamin D levels may increase the risk of developing cancer, hypertension, stroke, and quite possibly, dementia.

The most promising evidence for the role of vitamin D in cognitive decline seems to come from two studies reported during the 2010 Alzheimer's Association International Conference. These studies have presented strong evidence that low vitamin D levels are not good for the brain. Low vitamin D levels are extremely common in elderly patients because of reduced dietary intake and sun exposure.

In a study based on analysis of data from the Third National Health and Nutrition Survey (NHANES III), very low vitamin D levels were associated with a six-fold increase in risk for cognitive decline. According to testing conducted during the study, those who were mildly deficient had twice the risk of developing cognitive decline.[147]

Similar results were discovered during the Italian InCHIANTI study of 858 men and women over the age of sixty-five. This study found that those with the lowest vitamin D levels were at greater risk of declining scores on the Mini-Mental Status Exam as compared to those in whom vitamin D levels were sufficient.[148]

Older women may be more susceptible to declining cognitive function if their vitamin D levels are low, according to one recent study. When women with decreased vitamin D levels were compared with those with normal vitamin D levels, those with low levels were twice as likely to have low scores on a mental status questionnaire.[149]

Low vitamin D levels have also been associated with a greater risk of stroke and cerebrovascular disease, in addition to dementia, in older men and women.[150]

In contrast, one study looked at low vitamin D levels in a group of men sixty-five years of age and older. After having participants take two tests designed to measure cognitive function,

researchers found no relationship between low test scores and vitamin D levels.[151]

The human brain has vitamin D receptors, known as VDR receptors. Some association has been found between polymorphisms, or genetic changes, that may occur in these receptors and Alzheimer's disease, though very little is understood to date. When researchers looked at DNA from 255 individuals who had Alzheimer's disease and 260 individuals considered to be cognitively normal, the results suggested that vitamin D may play a role in the development of the disease.[152]

It may be that supporting vitamin D levels through supplementation will have an impact on preventing or reducing cognitive impairment, according to some studies, though not all are in agreement.[153]

Some argue that vitamin D is not a direct cause of dementia, but an indication of poor health that is found in common with Alzheimer's disease and other related conditions. More research is needed to clarify the role of vitamin D in the development of dementia.[154,155]

Solutions:

- Have your vitamin D_3 levels assessed.
- Supplement with vitamin D_3 for overall health.

Toxic Exposures

We've known for a long time that exposure to toxic metals and pesticides can have a bad effect on the body, from reducing the effectiveness of certain essential pathways to association with diseases like Parkinson's disease.

Research is now linking low-level exposure to lead and other toxic metals to health issues we know contribute to decline in mental function. The co-morbid conditions that result from exposure include high blood pressure, kidney, brain, and nerve damage. Iron, mercury and other toxic metals are potent neurotoxins that can contribute to neurodegeneration.[156,157]

In the Phytoner study conducted in southwest France, vineyard workers were enrolled in a study to see what the long-term effects are of exposure to pesticides. Out of 614 participants in the study who had worked in the agricultural business for twenty years or more, lower scores occurred in testing with those exposed to chemicals the most. At the beginning of the study in the late 1990s, those enrolled were forty-two–fifty-seven years of age. In follow-up MMSE testing four–five years later, all but two of those exposed to pesticides had worse cognitive testing scores than those who were not exposed. It is especially striking to note that in a study involving French individuals not exposed to chemicals and not diagnosed

with dementia, there was not a similar decline in MMSE scores over the same period of time.

Another follow-up in this study began in 2010, twelve years after the original data was collected. With some of the workers now approaching or over age sixty-five, there may be some cases of Alzheimer's disease identified in the group, which will provide better information about chemical and pesticide exposure over a long period of time.

While the data cannot be considered conclusive or final yet, the researchers involved say that the results obtained so far cannot be based solely on aging, especially in such a young group of people. Decline in cognitive function seems to be correlated with long-term exposure to pesticides and toxic metals.[158]

Another lifestyle factor that appears to be associated with doubling the risk of dementia and Alzheimer's disease is heavy smoking in midlife. If the patient has avoided getting cancer, or developing cardiovascular disease during his or her lifetime, then they may face an increase of cognitive decline. In this long-term observational study, those individuals who smoked two or more packs a day had a 100% increase in risk of dementia, while those smoking one–two packs of cigarettes a day had a 44% increased risk. On the other hand, those who quit smoking reduced their risk of development dementia to that compared to those who never smoked.[159,160]

Solutions:

- Have your heavy metals assessed.
- Take steps to reduce exposures to pesticides and heavy metals.
- Quit smoking.

Sleep Deficit

Sleep is an important component of normal brain aging, with many studies showing that lack of sleep increases mortality risk and risk of dementia. Lack of sleep decreases important hormones, such as growth hormone, increases obesity, and adversely affects coping and the ability to manage stress.

Sleep is important in ensuring that you remember new material, according to a study looking at the ways in which we store and find new information in the brain. The hippocampus is the place that we first deposit memories and they do not immediately become translated into retrievable information. When we are awake, the ability to commit these memories to long-term storage is affected by new information coming in. The theory that the researchers wanted to investigate in this study was whether sleep helped the brain to store information in the hippocampus, avoiding the loss of information that occurs during wakefulness.

When researchers evaluated twenty-four volunteers given cards to memorize, they found that

those who were allowed to sleep briefly remembered more information than those who were not allowed to sleep following the exercise. From this information, researchers contended that the inability to store short-term memories may be affected by sleep issues, leading to increased forgetfulness often associated with memory decline.[161]

In fact, central sleep apnea has been found in those with neurodegenerative diseases.[162,163]

Amyloid beta accumulation, which is found in high concentrations in those with dementia, may be affected by sleep-wake cycles as shown in animal studies. These studies found that wakefulness increased amyloid beta levels and sleep decreased them. Sleep deprivation over the course of three weeks was associated with rapidly increasing amyloid plaque deposits in mice. The conclusion is that the sleep-wake cycle has an impact on amyloid beta levels and sleep that becomes abnormal may be linked to the development of Alzheimer's disease.[164]

Solution:

- Develop healthy sleeping habits.

Immune Response and Infectious Agents as Triggers for Alzheimer's Pathology

For many years, scientists have suspected that the infectious agents, Herpes simplex virus 1 and Chlamydia pneumonia, may act as triggers for the development of Alzheimer's disease pathology.

This theory gained more momentum recently because of a Phase III clinical trial involving the drug, semagacestat, and the development of beta amyloid plaque in the brains of patients with Alzheimer's disease. The drug was designed to reduce beta-amyloid plaque buildup in the brain by interfering with the function of the enzyme gamma-secretase that makes it. In the trials, the drug not only did not reduce beta-amyloid plaque, it made participants in the study worse. The drug manufacturer, Eli Lilly, stopped the trial early as a result.

Beta amyloid is found in high concentrations in the brains of those with Alzheimer's disease. Many studies have focused on beta amyloid as the factor causing degeneration of the neurons in the brain. According to David Perlmutter, MD, this peptide, considered an antimicrobial peptide, may actually be acting in a defensive way rather than the causative factor.[165,166]

Many studies are now focusing on ways to support the immune system in its efforts to protect the brain from the damaging effects of beta amyloid.

Chlamydia pneumoniae is a bacterium most commonly associated with pneumonia and lung disease. More recently, research has associated this bacterium with the formation of atherosclerotic plaque leading to cardiovascular disease. Scientists have wondered if it could also be a trigger for the deposition of amyloid plaque in the brain, leading to neurodegradation and dementia.

In an animal study, *C. pneumoniae* was extracted from brain tissue with Alzheimer's disease and then mice were exposed to it to see if any disease would develop. Adding *C. pneumoniae* caused increased deposition of amyloid plaque and pathologic changes without any type of genetic influence known. There are many interesting implications to this study and possible mechanisms by which *C. pneumoniae* might initiate brain changes in those most susceptible.[167]

Herpes simplex virus 1 is most known for its tendency to cause cold sore breakouts on the lips or in the mouth.

Solution:

- Support your immune system to resist infection.

Thyroid/Iodine Deficiency

Low or high levels of TSH, or thyroid-stimulating hormone, may be a risk factor for developing Alzheimer's disease. In a study of 2,000 patients associated with the Framingham Study, researchers found that a TSH below 1 or above 2.1 was more strongly correlated with Alzheiemer's disease in women. There was no association noted in men. These values were the same regardless of whether the study volunteer was taking thyroid replacement hormone or not. Researchers could not determine whether brain changes had already occurred before there was a change in the TSH level or not.

What this study suggests is that a more narrow control of thyroid hormone is important to reducing cognitive changes and that imbalance in thyroid levels may contribute to cognitive decline.[168]

A deficiency of iodine can also contribute to risk of mental changes and dementia. Most of our understanding about the importance of iodine in the body is related to the thyroid gland, where it is essential for the production of thyroid hormone. The fact is, however, that up to 70% of the iodine we consume is absorbed in other tissues. The salivary glands, gastric mucosa, breast tissue, and kidney all have iodine receptors that are important for maintaining health. Low levels of iodine in the body may lead to many problems, including goiter, underactive thyroid, breast cysts and breast cancer, and possibly dementia.

Iodine is primarily available from seafood sources, such as seaweed, fish, and shellfish, and in minor amounts in milk and dairy products. It is also available through supplementation. Despite the availability of iodized salt, most people are low in their intake of iodine. Amounts established for intake, while useful for preventing goiter, and not adequate for the levels needed by the body for optimum health.

Solutions:

- Maintain a properly balanced thyroid hormone level.
- Supplement with iodine.

Calcification

One of the hypotheses about the development of Alzheimer's disease involves the process of calcification. In the normally aging brain, the body is able to to maintain an adequate balance of calcium. In the abnormally aging brain, however, two proteins are believed to interfere with the process of calcium balance to allow too much calcium to be released. Excess calcium can cause damage to neurons, leading to neurodegeneration, inflammation, cognitive decline, and memory loss.

In the vessels, calcium is an indication of chronic vascular disease. When calcification occurs in major blood vessels, it can be associated with vascular disease occurring in the brain and poses a risk factor

for dementia. When other risk factors, like smoking history, high blood pressure, and diabetes, are present, this adds to the potential for brain changes.[169]

In a recent study, vitamin D intake was shown to reduce dementia risk, whereas excess calcium intake was shown to damage brain arteries and lead to increased risk of brain lesions.[170,171]

Solutions:

- Maintain adequate levels of vitamin D.
- Take the correct amount of calcium, balanced with magnesium.

Fatty Acid Imbalances

Omega-3 fatty acids appear to be even more important than previously thought to maintain healthy cognitive function, according to recent studies. Adequate intake seems to be important for maintaining synaptic connections in the brain, which was identified in a study involving DHA, a marine source of omega-3 fatty acids.[172–174] Increased brain aging occurs when intake of ,essential fatty acids is low.

In a study conducted at UCLA, increased blood measurements of omega-3 fatty acids were associated with better functioning on cognitive tests and decreased brain volume shrinkage, a process that occurs with aging. Those with lower levels of omega-3 fatty acids in their blood had brain volume

shrinkage that was accelerated by two years of aging. Researchers speculate that increased intake of omega-3 fatty acids may support vascular health, reducing blood pressure and inflammation in the body, thus decreasing Alzheimer's disease risk.[175]

Omega-3 fatty acids also appear to stabilize atherosclerotic plaque, reducing cardiovascular incidents. Stable plaque is more desirable than unstable plaque, which can rupture and cause cardiovascular damage. Study results show that atherosclerotic plaque may be more affected by dietary changes than previously thought.[176]

Solutions:

- Maintain an adequate intake of essential fatty acids daily.
- Take 1000 mg of DHA daily for brain health. (Check with your doctor if you are on any blood-thinning medications before taking essential fatty acids.)

DNA Gene Mutations

DNA genetic mutation may predispose individuals to the development of Alzheimer's disease and dementia. This is an area of recent exploration to improve upon our understanding of the genome and what happens in the development of dementia.

Some of these genetic variations, such as the SORL1 gene (a receptor for apolipoprotein E), may predispose the brain to accumulate the amyloid

precursor protein, APP, which is implicated in the pathogenesis of Alzheimer's disease. Increased neurotoxic insult may result along with the formation of more neurofibrillary tangles.

Neurofibrillary tangles that contain more toxic levels of amyloid beta have been found elevated in familial Alzheimer's disease and sporadically in others and is associated with early onset, usually before the age of sixty-five. This type of Alzheimer's disease is associated with mutations in one of three genes in 50% of cases.

Three genes have been identified as risk factors for the development of Alzheimer's disease, all of which are dominantly inherited. The earliest gene to be identified is the gene coding for the lipoprotein known as apolipoprotein E or APOE, found on chromosome 19. This lipoprotein affects a specific lipoprotein in the body known as VLDL, or very low-density lipoprotein. We all have some amount of APOE because it helps transport cholesterol in the bloodstream to the liver, where it is used. There is a specific type of APOE, however, which is known as APOE e4, and only 15% of people actually have this type. APOE e4 substantially increases the risk of Alzheimer's disease in those who have the gene and decreases the age of onset. In contrast, those with the APOE e2 gene have a decreased risk of developing Alzheimer's disease.[177,178]

While we don't completely understand why there is an increased risk with certain genetic alleles, it

appears that family history and other environmental influences play a role. The APOE e4 gene seems to be associated with an increased amount of amyloid beta plaque buildup in the brains of those affected with Alzheimer's disease and this plaque buildup is toxic to neurons.[179–181]

Non-Digestive and Digestive Enzyme Imbalance

As we age, we experience changes in our ability to digest nutrients, leading to chronic illnesses. When stomach acid and digestive enzymes are deficient in the body, it can affect our ability to absorb nutrients requiring acid and other co-factors to break them down into assimilatable molecules. Indigestion seems to be epidemic, with many who are experiencing chronic indigestion and reflux and difficulty absorbing nutrients, which then lead to deficiencies in essential fatty acids, proteins, and other important nutrients.

Non-digestive enzyme imbalance occurs in the brain and liver, leading to destruction of cells and memory loss.

Solution:

- Have stomach pH assessed.
- Supplement with betaine hydrochloric acid (hcl) and digestive enzymes.

Excitotoxicity

One of the most important neurotransmitters in the brain is glutamate, which enables brain cells to communicate with each other. Abnormal levels of glutamate, however, can cause excitability of nerve cells at the N-methyl-D-aspartic acid (NMDA) receptors in the brain. Excitability of nerve cells causes damage to those cells by allowing calcium to enter the cells, impairing their ability to communicate with each other, leading to cell death and the loss of synaptic connection. It is the loss of synapses that leads to memory loss.

One of the pharmaceutical strategies for excitotoxity is the drug, memantine, which targets glutamate receptors and improves signaling and protects the synaptic connections between nerve cells.

Cholesterol

Research has found that abnormal levels of cholesterol and poor cholesterol metabolism may be underlying factors in the development of Alzheimer's disease. Having high levels of the favorable cholesterol molecule, HDL, may be important to support and retain good memory and cognitive function.[182,183]

Serum LDL cholesterol levels were higher in patients with dementia and serum HDL cholesterol levels were lower according to one observational study.[184]

At least one study has suggested that an impaired cholesterol transport mechanism in the brain may be one of the factors leading to dementia and Alzheimer's disease. Though cholesterol comprises only 2% of the body, the brain contains 25% of the total body level. Cholesterol serves many purposes in the brain, including as an antioxidant, a component of the cell membrane, and an electrical insulator. It's also important for proper function in the synapses and in the support of neurotransmitters.[185] Authors of the study maintain that the recent trend toward a low-fat diet may be a factor in the development of Alzheimer's disease in that it lowers beneficial fat intake and accentuates carbohydrate intake, which can increase blood sugar levels and damage neurons.

Having high HDL levels in men over the age of eighty-five was found to be very beneficial to longevity, according to one study. They found that a diet that was higher in saturated fats provided through the administration of coconut oil helped support high HDL levels.[186]

Periodontal Disease and Alzheimer's Disease

Inflammation is a frequent result of periodontal disease caused by pathogens. Increased levels of inflammation can contribute to changes in the brain, elevating the risk for vascular and cognitive changes.[187]

Anesthetics, Isoflurane and Halothane May Trigger Onset

There appears to be a connection between anesthetic exposure and the onset of cognitive decline. Anesthesia in certain populations, particularly elders, can lead to confusion, delirium and cognitive changes for long periods of time.[188]

5

What is Conventional Medicine Doing to Treat Dementia and Alzheimer's Disease? What Do Drug Companies Actually Say?

Drug Treatment Philosophy

CONVENTIONAL MEDICINE IS FOCUSED on fixing what is perceived to be faulty brain chemistry, rather than preventing what many suspect is the real cause of Alzheimer's disease—brain poisoning—from a variety of causes, including heavy metals and poor diet leading to health issues like hypertension and diabetes that cause brain-altering inflammation.

Drug research has taken several directions since the first drugs were developed for the treatment of Alzheimer's disease. The first is focused on reducing symptoms and providing relief to patients. The second major direction is focused on disease-modifying drugs, those that reduce or prevent the deposition of amyloid beta and tau proteins in the brain or act at some other point in the development of this disease.

Drug Categories

Cholinesterase Inhibitors

One of the biggest areas of research in conventional medicine has involved the brain chemical, acetylcholine, which is often found in low amounts in the abnormally aging brain. It's a brain compound believed to be important in maintaining memory and fostering learning.

Many of the drugs that are being developed are acetylcholinesterase inhibitors (AchEI), which work by keeping the levels of acetylcholine high in the brain.[189,190] In addition to Alzheimer's disease, acetylcholinesterase inhibitors are used to treat other conditions, including myasthenia gravis, glaucoma, and postural tachycardia.

Four acetylcholinesterase inhibitors have been approved for the treatment of mild-to-moderate Alzheimer's at differing stages of the disease.

In 1993, the first of the anticholinesterase inhibitors, tacrine (brand name, Cognex®), was

developed and taken off the market ten years later because it caused severe liver problems (hepatoxicity) in patients. It is still in use, but rarely used due to its potent side effect. In addition, the side effects at the doses needed to be effective are not tolerable for the majority of patients using it. Studies ultimately showed that the drug did not work either.[191]

Three other anticholinesterase inhibitor drugs are still being used in the treatment of Alzheimer's disease. Each works on the same principle of keeping acetylcholine levels high by inhibiting the actions of the enzyme, acetylecholinesterase, which breaks down the neurotransmitter acetylcholine. By stopping this enzyme from working, acetylcholine levels are kept high in the brain. These drugs are: donepezil (brand name, Aricept®); rivastigmine (Exelon®); and galantamine (Reminyl®). Since their inception, several studies have been conducted on the relative effectiveness of these drugs. An independent clinical trial studying Aricept® concluded that it worked, but it had minimal benefits. Essentially, researchers concluded that "Patients and their families would probably notice no difference if the drug was stopped."[192]

Despite many negative studies, research is still being generated that advocates the use of these drugs, often in combination with other medications. The Cochrane Dementia and Cognitive Improvement Group's Specialized Register looked

at thirteen randomized, double-blind, placebo-controlled trials of the anticholinesterase inhibitors in current use.

They concluded that the three best-known drugs were effective when used in the treatment of mild-to-moderate Alzheimer's disease. They concluded that, though no one can identify the patients mostly likely to benefit, all three worked similarly and effectively.[193–199]

Another comparison of the literature concluded that these cholinesterase inhibitors may slow or stabilize decline in mental changes, behavior, and overall symptom expression as compared to placebo without clear indication of greater efficacy for any of them. Some suggest donepezil and rivastigmine may be a little more effective than galantamine. Researchers conclude that additional study is needed to determine whether these observations are valid.

Donepezil

Donepezil, brand name Aricept®, is indicated for severe Alzheimer's symptoms, though it is widely used to treat mild to moderate dementia symptoms, study findings conflict about its effectiveness.[200] In some studies, donepezil is reported to be no better than placebo in improving patient symptoms.[201] One randomized, placebo-controlled study demonstrated it was not cost-effective and that it had minimal overall benefits.

In a recent study in patients with moderate to severe Alzheimer's disease, researchers found it effective in treating moderate to severe symptoms, continuing its use in those with mild to moderate disease. The study was conducted with 295 nursing home patients who had been treated beyond the time donepezil is usually used (patients had to be on donepezil for at least three months). Researchers noted that those patients who were continued on donepezil showed improvement in their ability to understand, communicate and manage activities of daily living for up to a year longer than those patients who were not continued on the drugs. Family, caregivers and even patients reportedly noticed these improvements.

The research was intended to provide additional guidelines to doctors and caregivers regarding treatment, since the drug is often withdrawn as the disease progresses due to side effects and physiological tolerance.[202]

Rivastigmine (Exelon®)

Because of the side effects that occur with rivastigmine, it's sometimes recommended to take the drug with food so as to minimize its side effects—nausea, vomiting, and other gastrointestinal symptoms. It is also used as a patch, the transdermal system of administering drugs. This method delivers a specific amount to the system to maintain blood levels and bypass the liver, stomach and intestines.

It also gets around the problem encountered with administering drugs to patients with cognitive impairment, since it is easier to dose with a patch than a pill that has to be remembered one or more times a day. As the disease progresses, swallowing can be impaired, too, and it makes giving the drug easier in these cases.

While there may be some limited benefit using rivastigmine, long-term benefit is not established.[203]

Galantamine (Reminyl®)

Galantamine began as a derivative of plants but is now offered primarily as a synthesized drug. The naturally occurring supplement, galantamine, which is still based on plant medicine, will be discussed further in the natural therapy section.

Essentially, galantamine is an acetylcholinesterase inhibitor that has been touted for its benefit in mild to moderate cognitive impairment and has not been extensively studied for moderate to severe impairment. Studies claim benefit in drug trials of three, five, and six months in length. It is comparable to the other anticholinesterase inhibitors, donepezil, rivastigmine, and tacrine in action and side effects. It's known to produce acute gastrointestinal symptoms and is less tolerated at higher doses. In study trials, participants were more likely to stop their participation at doses above 24 mg as compared to those who were being treated with lower doses or placebo.[204]

Side Effects of Anticholinesterase Drugs for Alzheimer's Disease

The approved anticholinesterase drugs are tacrine, donepezil, rivastigmine, and galantamine. The side effects they are most noted as causing are nausea and vomiting, diarrhea, weight loss, and dizziness, which have been reported in all of the studies of them. The reported side effects are lowest in donepezil and highest in rivastigmine.[205] An increased number of deaths have been reported in some studies with the use of the anticholinesterase inhibitors.[206]

Transdermal, or through the skin, application of rivastigmine apparently increases tolerability.

Other side effects reported from this class of drugs are liver toxicity, gastric problems, high or low blood pressure, fainting, increased heart rate, shortness of breath, cataract development and blurred vision, bowel incontinence, and seizures and tremors. Mental emotional changes that have been reported include aggression, irritability, confusion, nervousness, restlessness, depression, and crying.[207]

Another, more alarming trend, is the pressure to use acetylcholinesterase inhibitors on healthy adults with a focus on preventing progression to dementia or Alzheimer's disease. An interesting study looked at this trend, using a battery of cognitive testing and EEG measurements. The study showed harmful effects in healthy adults between the ages of fifty and seventy, and most pronounced

for those in their fifties, with very slight benefit in those over age seventy. The study authors caution that administration of these drugs needs to be based upon assessment and geared to the individual, rather than prescribed due to the faulty assumption that they may confer benefit in all people. Within their study methods, they describe testing that may be conducted to determine potential benefit before administration.[208]

Secondary Prevention—Drugs that Are Intended to be Disease Modifying

Amyloid Inhibitors

Many studies are focusing on secondary prevention through decreasing production of Abeta, clearing it when formed, or preventing it from aggregating into plaque.[209] The goal of this strategy is based on the assumption that the accumulation of the Abeta and tau proteins causes oxidative stress in the brain, neuronal destruction, and then the clinical expression of dementia and Alzheimer's disease. The goal is to slow these processes of destruction down.

NMDA Receptor Antagonist

Memantine (Namenda®)

Memantine is a former influenza drug that has been refocused for the treatment of Alzheimer's

disease. It is an N-methyl-D-aspartate (NMDA) receptor antagonist with low to moderate affinity for these receptors. This drug appears to be useful in the protection of neurons from abnormal levels of glutamate, which causes excitotoxicity. It is approved to treat those with moderate to severe Alzheimer's symptoms and may have some modest improvement on cognition. The fact that it reduces abnormal brain activity means that it may have some positive effect on behavior.

Many drugs used in the treatment of dementia are very toxic and not safe. Since memantine has been used for many years, its advantage is that it has a safe profile and saves a lot of time normally spent in drug development.

One of the most important neurotransmitters in the brain is glutamate, which enables brain cells to communicate with each other. Abnormal levels of glutamate, however, can cause excitability of nerves cells. Excitability of nerve cells causes damage to those cells and impairs their ability to communicate with each other, leading to cell death and the loss of synaptic connection. It is the loss of synapses that leads to memory loss. Memantine works on glutamate receptors and improves glutamate signaling and, as a result, protects the synapse between nerve cells.

In a trial of memantine, which was stopped early, there was some improvement in memory, particularly recognition of family members.

While some improvements have been noted, most results are considered clinically marginal.[210]

It is not considered a "cure" but a step in the direction of improvement, with research being done to perfect other drugs based upon the actions of memantine. Some of these are called nitromemantines, a combination drug consisting of both memantine and nitroglycerine.[211,212]

The results of a drug trial of memantine showed "no significant differences between memantine and placebo for the number of dropouts and total number of adverse effects, but a significant difference in favor of placebo for the number who suffer restlessness."[213,214]

A subsequent trial showed that memantine may have a slight beneficial effect in patients with moderate to severe Alzheimer's disease at six months. Any beneficial effect in cognition in those with mild to moderate vascular dementia was not clinically detectible but identifiable in those with Alzheimer's disease.[215]

Memantine is being increasingly used in a combination therapy along with a cholinesterase inhibitor drug that increases acetylcholine in the brain.

While the drug is well tolerated, the most frequently reported adverse events were dizziness, headache, and confusion.[216,217]

Other Inflammatory Modulators Being Considered

Etanercept (Enbrel®)

Enbrel® is a drug, originally used for arthritis, which is being repurposed for use with Alzheimer's disease, though its safety is unknown and may have some MS-like effects in some patients. It's been noted to produce cognitive improvement, sometimes within a short period of time after administration. In one study, this drug was given once a week to patients with mild to severe Alzheimer's disease in doses of 25–50 mg and improvement was noted over the course of six months. The major disadvantage is that it is administered through spinal injections, which are risky. Very little additional research has been done regarding its possible use with dementia and Alzheimer's disease.[218]

Statins

Statins are being studied for use as a possible therapy to slow the progression of dementia and Alzheimer's disease, but not neuronal degradation.[219,220] Many report increased memory problems with statin drug use, however, even without a diagnosis of dementia or Alzheimer's disease.

The rationale for using statins is related to research that links high cholesterol levels in the brain with increased deposition of amyloid beta in the brain, increasing risk of Alzheimer's disease.

Outcomes of studies are extremely variable, however, and there is no consensus about benefit.[221]

Intensive use of statins, however, has been shown in studies to increase the risk of developing diabetes.[222]

Amantadine (Symmetrel®)

Amantadeine is a dopaminergic drug used in the treatment of Parkinson's disease that may show some benefit in very specific ways in the treatment of Alzheimer's disease and dementia. It's been used to reduce behavioral disturbances in patients with frontotemporal dementia and to improve mental status in end-stage Alzheimer's disease.[223]

Nicotine Patch

Nicotine patches have been studied as a possible therapy for those with mild cognitive impairment. In a recent study, 15 mg doses were administered through the skin (transdermal application) to 74 nonsmoking volunteers who showed signs of mild cognitive impairment over the course of six months.

Study volunteers showed improvement in memory, attention and speed of response and the therapy was well tolerated. The results, however, were not rated as having clinical significance, suggesting more study needs to be done to determine whether this is an effective long-term strategy.[224]

EpoD and Bexarotene

The two cancer drugs, epoithilone D (EpoD) and bexarotene may have benefit in the treatment of Alzheimer's disease, as shown in animal studies. EpoD enters the brain and targets the mechanism involved with deposition of tau protein. This drug appears to stabilize the microtubules involved in tau protein deposition and reduce tau protein tangles, reducing neuronal damage and cognitive dysfunction.[225]

Bexarotene is an anti-skin cancer drug that appears to clear amyloid beta protein from the brain, increasing cognitive function. Animal studies showed that the drug improved function within seventy-two hours of treatment and reduced plaque by up to 75% by the end of treatment. Results of these studies are very promising for the treatment of Alzheimer's disease and dementia.[226]

Why Conventional Therapies May Make It Worse

Drug Treatment Fallacies

One of the fallacies of treatment for dementia and Alzheimer's disease is that there is going to be one solution to the problem of cognitive decline.

There are so many factors influencing the development of dementia, from lifestyle issues to the many

health concerns affecting elders that it is highly unlikely that there will be one single drug therapy that will stop its progression. Those with cardiovascular disease, cancer, diabetes, and atherosclerosis may also have difficulty eliminating drugs from the system, so drug interactions and toxicities become a major concern in any care program.

In addition, those with the highest risk factor, the APOE e4 gene carriers, are least likely to respond to conventional treatments.[227]

Most of the drug therapies designed for dementia are not cost effective, with less than 20% of patients even responding moderately to conventional treatments that cause many drug reactions.

In a recent review of therapies directed at Alzheimer's disease, researchers concluded that the effects of these drugs were minimal, not justifying their expense or side effects.[228]

Many have lamented that so many of these studies have been conducted by the drug industry itself, with few independent studies done.

In the United Kingdom, the National Institute for Clinical Excellence (NICE) refused to fund donepezil, rivastigmine and memantine, Alzheimer's drugs that were intended to be used in the early stages of the disease. Their initial decision was issued in 2006, and guidelines were reaffirmed in August 2009.

NICE more recently created new guidelines for using these drugs in the treatment of Alzheimer's

disease in England and Wales. Patients will have access to the top anticholinesterase drugs, Aricept®, Exelon® and Reminyl® during early to moderate disease. There is another drug, Ebixa® that people will have access to for late stage disease or instead of the anticholinesterase drugs if they cannot take them. The Alzheimer's Society supports this decision in the belief that up to 50% of people who take them benefit from them, despite the lack of cost effectiveness and adverse effects experienced by many.[229,230]

6

There Is a Better Way

NO MATTER WHAT THE scare tactics are or the risk factors you may think you have, there is a better way to managing brain aging than those promoted by conventional drug company sources. The natural approach, especially when focused on prevention, is the best approach. Among the recommended strategies are dietary and lifestyle changes, bio-identical hormone replacement, supplements and botanicals known to improve cognitive function, and continuous and varied mental stimulation.

The goals of natural medicine's approach to preventing dementia and Alzheimer's disease are to:

1. Prevent the physical changes that occur by reducing risk factors causing plaque formation and degradation of neurons.

2. Find ways to reduce and remove any harmful plaque already there.
3. Support your brain function through regeneration of nerve pathways.
4. Reduce the risk of further brain injury by increasing antioxidants.
5. Support mental function long into later years through brain training and stimulation.
6. Improve mental function in those who already have Alzheimer's disease.
7. Reduce exposure to environmental causes, toxic metals, and food choices that are known to be risk factors.

Here's What You Can Do to Begin a Therapeutic Lifestyle Strategy Now

While there are no established cures for age-related dementia and Alzheimer's disease, there are things you can do to reduce your risk of developing them. In truth, such an approach is based on living a healthy lifestyle based on good health choices. If you already have symptoms, there are things you can do to retard its progression.

Any program that you begin will be focused on improving lifestyle and diet, improving environmental factors that increase risk, and modifying genetic risk factors, such as family history and at-risk genotypes.

Your Strategy for Natural Prevention

If you are motivated to begin a program to protect or even enhance your mental capacities, you have probably already realized that there are many factors that affect it. Don't wait for science to come up with a solution, since it may not be coming soon and it may be too late to reverse damage that is undetected and accumulating. Remember, by the time symptoms of cognitive decline are apparent, significant neurological damage has already occurred.

Start with the Basics

Get a good night's sleep, eat a good diet full of antioxidants to protect you against free radical damage, balance hormones, correct thyroid and adrenal function, and maintain a healthy blood pressure and blood sugar. Exercise both the brain and the body daily.

Everything you do that reduces inflammation, free radical exposure, and preserves the integrity of cell membranes will reduce your risk of developing dementia.

One recent study has demonstrated that this type of prevention, indeed, may have significant benefit in reducing overall risk. When 1,200 participants between the ages of sixty and seventy-seven with high risk for developing dementia were enrolled in the study, researchers focused

on nutrition, exercise (both cardiovascular and strength building), cognitive training, and management of health issues. Preliminary findings suggest that reducing risk, even slightly, will have a significant and positive impact on cognitive function.[231]

Diet and Nutrition

Diet is a significant factor in any brain health program. Many studies are now showing that healthy brain aging is affected by what we eat. While it may seem intuitively obvious to eat the best diet that one can, there are some nutrients that can and should be emphasized in any neuroprotective program.

In a very comprehensive and interesting study, the dietary patterns of 2,148 elders without dementia and living in New York were assessed. Dietary patterns were rated for relative risk of developing dementia and a distinct dietary pattern emerged as being protective.[232]

To reduce Alzheimer's risk, the most beneficial diet included one that was rich in dark and green leafy vegetables, cruciferous vegetables (broccoli, brussel sprouts, cauliflower), tomatoes, nuts, fish and poultry, and salad dressings containing healthy oils such as olive oil. At the same time, reducing the amount of red and organ meats, butter, and high-fat dairy products was also protective.

The goal of such a diet is to reduce the intake of saturated fats and improve the intake of

monounsaturated fats, such as olive oil, and include adequate amounts of omega-3 fatty acids. Such a diet also maximizes intake of omega-6 polyunsaturated fats, vitamins E, B_{12} and folate, low levels of which are often associated with dementia and cognitive dysfunction.

While the benefits of a wholesome, nutritious diet may be obvious to many, the relative benefits of such a diet for the brain have not been demonstrated until recently in other studies. Several studies have shown that the Mediterranean diet, which emphasizes an intake of healthy fruits and vegetables, protein, healthy oils and modest amounts of alcohol, can help increase mental function and slow decline in cognitive function. This is true even after all the possible risk factors have been assessed, including high blood pressure, smoking, being overweight, and other health issues. Those who adopted the Mediterranean diet were at least two years ahead of those who had not in the study, according to one lead investigator.[233–236]

Similar results were found in another study of 1,880 elders who adopted the Mediterranean diet and increased physical exercise. Incorporating both diet and exercise in a daily routine reduced risk of developing Alzheimer's disease when compared to those who did not adhere to the diet or participate in any kind of exercise or physical activity.[237–239]

To reduce cognitive decline, there is a protective benefit to eating three or more servings

of vegetables a day. Memory loss was reduced by up to 40% in those following this dietary recommendation.

Fresh vegetables appear to preserve brain function by an additional five years later in life. In a study involving 3,400 volunteers, green leafy vegetables had the best neuroprotective effect in older individuals. Fruit consumption was not as strongly correlated with cognitive benefits.[240,241]

Carotenoids, the fat-soluble antioxidants in food, appear to protect polyunsaturated fatty acids (PUFAs) such as omega-3 fatty acids, from oxidation in the body. This is important for protection from Alzheimer's disease. There is an association between higher carotenoid levels and higher DHA levels and better Mini-Mental Status Exam scores (MMSE).

This information suggests that, when considering diet and nutrition, it's important to target multiple specific nutrients, such as lutein, beta-carotene, and DHA, to most effectively slow the rate of cognitive decline.[242]

When individuals maintain a close adherence to the Mediterranean diet and have a physical exercise program they follow, there is a much lower risk of development of Alzheimer's disease when compared to those who do not follow the diet or participate in any type of exercise program.[243–245]

Benefits of Calorie Restriction

An important component of reducing the risk may be lowering the body heat through a low-calorie diet.[246]

Among nongenetic factors, calorie restriction has very beneficial implications for reducing overall risk for plaque burden. There may be a connection between high saturated fat intake, a high caloric diet, and increased beta amyloidosis. Dietary changes and calorie restrictions may reverse this trend.

Indeed, studies with animals have shown that calorie restriction may be helpful in Alzheimer's disease by preventing amyloid-beta accumulation. In the studies, a calorie restriction of 30% showed reduced levels of two types of harmful plaque (Abeta) when compared to normally fed animals.[247]

Caloric restriction is also a beneficial strategy for maintaining a healthy weight into midlife and reducing the risk posed by obesity. Overweight patients have a 35% greater risk of developing Alzheimer's disease and dementia and with obesity, this risk jumps to a whopping 74% increase in risk.[248] When combined with diabetes, the obesity risk factor jumps to a greater than four-fold increased risk.[249,250]

"Choices we make every day have a major impact on how our brains age," says Dr. Gary Small, Director of UCLA's Longevity Center. "In fact, physical

exercise probably has the most compelling evidence that it can lower the risk of Alzheimer's."

"We're not saying that we can definitely prevent it in everyone, but the goal is to stave off the symptoms, sometimes for years, and for many people, that may mean never getting the symptoms in their lifetime." Source: CNN Health, March 8, 2012.

Exercise

"Choices we make every day have a major impact on how our brains age," says Dr. Gary Small, Director of UCLA's Longevity Center. "In fact, physical exercise probably has the most compelling evidence that it can lower the risk of Alzheimer's."

"We're not saying that we can definitely prevent it in everyone, but the goal is to stave off the symptoms, sometimes for years, and for many people, that may mean never getting the symptoms in their lifetime." Source: CNN Health, March 8, 2012.

Even a little exercise seems to have a benefit for memory and can slow the progression toward dementia and Alzheimer's disease. Lack of activity, on the other hand, is associated with susceptibility to dementia pathology in the brain. In an animal study, buildup of amyloid plaque was associated with resting behavior in the "default-mode network" of the brain. Times of rest were connected to time of amyloid plaque accumulation,

reduced metabolism of glucose, and brain atrophy in the least active parts of the brain.[251]

An Australian study in which volunteers exercised only twenty minutes a day showed that there was improvement in memory in those over the age of fifty. While no one in the study had dementia, all of the participants said that they had memory problems. They were instructed to do at least 150 minutes of moderate exercise a week and then were tested both before and after the study period. When results were compared, improvement was evident on the test scores.[252]

This concept has been studied for many years through the Nun Study, begun by David Snowdon, PhD, in the 1980s. In this classic, long-term study of nuns in a relatively controlled environment, Dr. Snowdon found that there were benefits to exercise even in those nuns who later showed signs of Alzheimer's on autopsy.[253]

Exercise improves many things, including how the body uses glucose, reduces blood pressure, and increases mental function.[254] Snowdon found that in nuns who had started exercising, even as late as seventy, Alzheimer's disease was slowed or even prevented.

In his book, Dr. Snowdon reports that one of the nuns started walking at age seventy though she had never done this before. When she died many years later without any symptoms of dementia or Alzheimer's disease, her brain showed

the classic signs of beta-amyloid and tau protein, typically found in the brains of those afflicted. The only conclusion that seemed obvious was that the walking prevented cognitive decline and the expression of symptoms.

In fact, one study has quantified the amount of walking that helps maintain memory and brain volume in elders. There was an association between walking a mile a day and preservation of brain volume nine years later, with reduced risk of dementia thirteen years later. Those who had walked at least an average of seventy-two blocks, which was about six–nine miles a week, had a higher volume of gray matter than those who had not walked as much. While walking more than this was beneficial, walking at least seventy-two blocks was necessary to detect increased brain volume. Researchers concluded that there was an interesting association between the level of physical activity done as walking and the preservation of brain volume and structure, leading to a reduced risk of developing dementia.[255]

Aerobic exercise may help support cognitive and functional capacities by modifying changes in the brain,[256] reducing the risk of Alzheimer's disease,[257] and increasing cerebral profusion.[258,259]

Early diagnosis is important because symptoms of dementia and Alzheimer's disease respond best to treatment in the early stages. Recent studies

show marked changes in brain oxygenation during mental and physical tasks.[260]

One study compared the effects of exercise as a comprehensive routine for patients with severe Alzheimer's disease and found a definite benefit.[261]

A new study suggests that "exergaming" (combining exercise on a stationary bicycle with cognitive stimulation through virtual reality tours) enhances learning the most in elder adults with cognitive decline.[262]

Reduce Cardiovascular and Blood Sugar Factors

To reduce cardiovascular risk factors, it's important to maintain a healthy coronary artery blood flow to protect the heart and vessels and avoid the buildup of damaging atherosclerotic plaque.

Keeping levels of the omega-3 fatty acids EPA and DHA elevated are important to support brain-derived neurotrophic factor—BDNF—a compound that encourages nerve cells to grow and make new connections. When rats with brain injuries were fed fish equivalent to two fish servings a week, they improved to the level of those animals without brain injuries; animals produce it when they exercise. Eating a diet rich in omega-3 fatty acid could have some of the same neurological effects as exercise. Supplementing food with the omega-3 fatty acid DHA can dramatically slow neurodegenerative symptoms.[263]

Curcucmin has also been shown to reduce Abeta accumulation in the brain. Mice that were fed the equivalent of the daily intake of individuals living in India had half as many beta amyloid plaques. Curcumin binds to amyloid beta protein, discouraging them from aggravating.

A key point is that fish oil and curcumin prevent neurodegenerative disease with fewer side effects than drugs.

When antihypertensive drugs are needed to control elevated blood pressure symptoms in those with mild to moderate Alzheimer's disease, angiotensin converting enzyme (ACE) inhibitors have shown the ability to slow progression of the disease.[264] These effects in people without hypertension have not been studied.

People with metabolic syndrome are more likely to be diagnosed with Alzheimer's disease at an earlier age than those individuals who do not have metabolic syndrome, according to some studies. Maintaining a healthy blood sugar level, weight, and blood pressure is important to reducing overall risk of developing cognitive decline.[265]

Solutions:

- Keep homocysteine levels low by taking supplemental vitamin B_{12} and folate.
- Take vitamin C and flavonoids.
- Seek treatment for diabetes.

Correct Hormonal Deficiencies with Gender-Specific Bioidentical Replacement Therapy (BHRT)

The higher prevalence of Alzheimer's disease in women when compared to men suggests a gonadal connection. Research evidence supports the role of estrogen in brain regions that are associated with learning and memory and the protection of cholinergic neurons, those known to degenerate in Alzheimer's disease. Hormonal therapy may decrease the risk or delay the onset of symptoms in postmenopausal women. Hormone replacement therapy, however, may not have an effect on those who already have the disease.[266]

Bone mineral density measurements may be another way of establishing risk for Alzheimer's disease. Bone mineral density measurement may be a surrogate marker for estrogen exposure associated with cognitive performance and risk of cognitive decline. In one study, low femoral bone mineral density was associated with twice the risk of Alzheimer's disease and dementia from all causes in women, though not men, and suggests that the amount of estrogen exposure over time may influence the risk of developing these diseases.[267]

Maintain a Healthy Mind

Mind activities, such as reading books, playing cards and board games, doing crossword puzzles, and maintaining higher levels of education

are important activities to prevent dementia and Alzheimer's disease.[268,269]

Many studies now show that creativity and lifelong learning have protective effects, both before Alzheimer's disease onset and in patients who have Alzheimer's.[270]

Among the best ways to maintain cognitive function throughout the lifespan are to reduce stress, do memory exercises, develop a healthy lifestyle, and engage in regular physical fitness. In a study involving 115 older adults with an average age of eighty-one, a combination of mental exercises and implementation of a healthy lifestyle had a significant effect in just six weeks. Participants in the study showed improvement on testing when they participated in a brain fitness memory-training program.[271]

Maintain a Healthy Support System

Being socially active and maintaining a healthy support network is associated with decreased risk of Alzheimer's disease and dementia. Studies show that when individuals participate in a diverse pattern of activities with a number of social outlets, their risk of cognitive decline is reduced. Activities like reading, visiting with relatives, going to events and movies, participating in sports activities, and leisurely walking are among activities positively correlated with mental health and brain function.[272]

Complex activities—both in work and social activities—are also supportive of brain health.[273]

Light to Moderate Alcohol Use May Be Protective Against Dementia

The evidence seems to be in; light to moderate consumption of alcohol, including wine, can protect against the development of cognitive changes in older individuals.

Recent studies are finding that light to moderate alcohol intake may help prevent dementia. While drinking alcohol in high amounts increases the risk of cognitive changes and impairment, drinking light to moderate amounts may be protective. Part of the benefit may be due to an improvement in blood vessels observed in those who drink alcohol.

While many studies have found that light to moderate alcohol intake may be helpful for young adults, it is quite another thing to find similar results in adults seventy-five and older. In this study of 3,202 German participants, the amount of alcohol that appeared to be most protective in the study was 20–29 grams. During the three years that the study was conducted, there was a 29% drop in risk for developing dementia in those who drank alcohol when compared to those who did not. While the types of alcohol were not rated for their individual ability to lower risk, the greatest hazard was associated with mixed alcoholic beverages.[274]

Similar findings have been reported in a study of older Chinese men and women in Hong Kong, with a mean study age of 79.9 years. Heavy drinking, which was determined to be consumption of more than 400 grams of alcohol in male drinkers and 280 grams of alcohol in female drinkers, was associated with a significant increase in risk for development of dementia. Mild to moderate intake of alcohol was associated with reduced dementia risk in study participants.[275]

This study also compared dementia risk with exercise and found that thirty minutes of exercise a day reduced overall risk by more than 60% when compared to the risk of those who did not exercise. Exercise of less than thirty minutes a day had close to a 48% reduction in risk for developing dementia.[276]

7

In Your Brain Healthy Lifestyle, Add In Specific Supplements with Exceptional Benefits

WHILE NO ONE CAN definitely say that eating a healthy diet full of fruits, vegetables, lean sources of protein, and healthy oils is going to prevent dementia, this type of diet is correlated with increased longevity and fewer disease processes. The same can be said of those who use supplements. Long-term supplement users are healthier than those who don't use any supplements or are taking only a multiple vitamin daily. These individuals are less likely to have hypertension and diabetes and show lower

levels of the inflammatory disease biomarkers and indicators of chronic inflammation, like elevated CRP and homocysteine and increased cardiovascular risk and stroke. These healthier individuals are also more likely to have optimal levels of triglycerides and good levels of HDL.[277]

Lithium

Lithium may have protective benefits against Alzheimer's disease. It's an element found in nature, occurring naturally in food. Most people know of it because it is used in very high doses in the treatment of bipolar disorder. Studies have shown that it supports the health of the nervous system. It's been shown to increase the volume of gray matter of patients with bipolar disorder up to 3%, a significant observation when studying brain health.[278]

When studied in patients with bipolar disorder, gray matter volume increased ten–twelve weeks into treatment with lithium and was supported through the total sixteen weeks of the study. A clinical response was observed as well.[279]

Using lithium over time seems to have neuroprotective benefits, reducing the risk of dementia.[280]

With these promising results, the possibility of using low-dose lithium in the prevention and treatment of dementia and Alzheimer's disease has been suggested and may be an easily used and overlooked treatment.[281–284]

Brain cells die in patients with Alzheimer's disease and other forms of dementia because they are diseases that affect important brain neurons, decreasing their function. Lithium may help support the proteins that are necessary in maintaining brain cell function, most especially those that protect us from chemical damage and ionizing radiation. In particular, lithium may help prevent neurofibrillary tangles that are formed from tau protein, one of the most commonly found abnormal proteins in the brain cells of those with Alzheimer's disease. Though tau proteins are found in small amounts in the normal brain, they are found in higher concentrations in those with dementia.

Tau proteins are made through phosphorylation, a process that commonly occurs in the body when one molecule is changed to another in a chemical pathway. The enzyme that does this, known as glycogen synthase kinase or GSK-3, is the enzyme inhibited by lithium. Researchers have suggested that this enzyme is the link between the formation of Abeta plaque in the brain and the neurofibrillary tangles formed of tau protein.

One recent study involving brain cell cultures reported that lithium kept brain cells alive, preventing early death of those cells. It is also possible it helps re-grow them after disease processes have occurred.

Another benefit of lithium orotate may be its ability to pull aluminum out of the tissues so that

it can be removed from the body. While its role in Alzheimer's disease is unknown, many have speculated that aluminum toxicity is a factor in its development.[285]

Niacinamide

Niacinamide is another nutrient that has shown considerable promise in the prevention of age-related brain changes, though very few studies have been done using it. Back in the 1940s, Dr. William Kaufman studied the use of niacinamide in the treatment of osteoarthritis and found it to be helpful in reducing symptoms. Dr. Abram Hofer found that niacinamide was beneficial in the treatment of schizophrenia.

Kaufman also found that symptoms related to memory, anxiety, and confusion cleared up using niacinamide.[286] A 2008 study involving mice conducted at the University of Irvine was very promising using the equivalent of 1500 mg of niacinamide a day.[287]

No definitive human studies have been done to date, however.

Increase Antioxidants

Much is said about the use of antioxidants for health, but little is said about how to use them and why. Oxygen, which we take in regularly through the lungs and transport through the blood to all tissues, is used in many metabolic processes in

the form of O2, or two oxygen molecules bound together. As part of those processes, molecules called reactive oxygen species, or ROS, are created from oxygen left behind in these processes as singlet oxygen—O—or only one oxygen molecule, not two. It is inherently unstable by itself and appears momentarily, looking for someplace to go. Although these reactions are normal in the body, it's important for free radicals to have somewhere to go to avoid them causing impairment. Antioxidants reduce the damaging effects of free radicals that cause age-related damage at the cellular level in the body.[288]

Why is this important? The damage caused by ROS can occur early, before anyone notices the symptoms of these diseases. They promote the accumulation of beta amyloid plaque and tau protein, leading to damage of important cellular processes. Once damage occurs, it can promote abnormal levels of lipids, proteins, nucleic acids and other compounds that are the result of a weakened cellular antioxidant protective system. It can even lead to increased permeability of the blood brain barrier (BBB), a cellular layer that protects the brain from injury by chemical processes. It's proposed that antioxidants may prevent some of this damage from occurring and increase survival.[289]

The antioxidants listed below are nutrients and minerals that may be obtained from food

or supplements. They are natural products that have been researched for their health-promoting benefits and possible protective benefits against the development of dementia and Alzheimer's disease. All support brain health and are important components of any anti-aging diet.

Curry, Turmeric, and Curcumin

Studies suggest that curcumin, the most active constituent in the Indian spice turmeric, may help protect the brain from Alzheimer's disease.

What evidence is there for its use in the treatment of dementia? Curcumin is derived from the root of the plant, Curcuma longa, and provides the yellow color in curry powder, commonly used in many Indian dishes. It is also an anti-inflammatory, a strong antioxidant, and has anti-amyloid properties, having been shown to protect against cellular damage caused by amyloid beta. It's also known as a metal chelator and immune modulator.[290–293]

It may have a beneficial effect in the treatment of Alzheimer's disease through its ability to affect macrophages. In one study, macrophages were unable to reduce levels of amyoid beta on their own. When turmeric was added, the herb restored macrophage function and the ability to destroy amyloid beta by switching on genes that had been switched off. Genetic function appears to be critical to macrophage function and without

this their ability to act is impaired. It is part of the toll-like receptor function of the immune system that enables immune cells to recognize invasion from pathogens and other deleterious compounds. Amounts used in the study were higher than one would consume naturally in food.

The question is why do macrophages become impaired in the first place?[294]

The Case for Supplementing with Vitamins B, C, D, and E

In a recent study of mental function and vitamin intake, four specific vitamins were shown to be very important. Blood levels of vitamins B, C, D, and E were measured in 104 men and women with an average age of eighty-seven during the study. Assessment involved brain scans to measure brain volume and cognitive skills testing. Those study participants with the highest levels of these four vitamins were found to have higher cognitive functioning and higher brain volumes, both critical to healthy brain aging.

The study also looked at levels of omega-3 fatty acids and trans fats. Omega-3 fatty acids were found to support cognitive function and promote healthy blood vessels in the brain, though did not seem to have an impact on brain volume, but trans fats were definitely correlated with shrinking brain size and poorer function on mental testing.

While results of the study do not indicate whether or not dementia would be avoided, as in all other aspects of risk, a healthier diet supports healthy brain health and aging.[295–298]

High Dose B Vitamins and Mild Cognitive Impairment

Brain shrinkage has been reported to occur early in the development of Alzheimer's disease. While the brain volume may shrink about a half a percent each year under normal conditions, it accelerates with the onset of Alzheimer's disease.

British researchers at the University of Oxford studied the use of high doses of vitamin B_{12}, folic acid and vitamin B_6 in 168 study participants who had mild cognitive impairment to see if they could help delay this process. These supplements are used to reduce homocysteine levels, a non-protein amino acid found in the blood that has been associated with cardiovascular disease and increased risk of heart attack. Elevated homocysteine levels have also been associated with the development of Alzheimer's disease. B vitamins (notably vitamins B_{12}, B_6, and folic acid) are frequently used to reduce homocysteine levels in the body.

When the results were analyzed, they showed that these supplements used in high doses stopped shrinkage of the brain by up to 50% when compared to those taking placebos. Results

like this suggest that B vitamin treatment might help prevent the onset of Alzheimer's disease during its earliest stages. While the study was not intended to check cognitive function, researchers said that those who were taking the supplements also scored better on tests designed to assess mental abilities.[299]

Low vitamin B_{12} levels could play a role in behavioral changes in Alzheimer's disease[300] and the etiopathology of dementia, leading to brain changes.[301–303]

Vitamin B_{12} used in conjunction with other therapies may have benefit, as well. Studies have looked into the effects of vitamin B_{12} on the daily, or circadian, rhythm in Alzheimer's disease. Participants in one study received bright light therapy for eight weeks. Half of the participants received vitamin B_{12} along with the bright light therapy. All involved in the study were evaluated using the Mini-Mental Status Exam (MMSE) after the fourth and eighth weeks.

What investigators found was that bright light therapy along with vitamin B_{12} improved vigilence level of participants during the day. Bright light therapy was also shown to improve the behavioral response and cognitive state during early Alzheimer's disease.[304]

Dietary Folate and Supplemental Folate, B_{12}

Low blood folate levels and elevations in homocysteine concentrations are associated with poor cognitive function. One of the reasons is that elevated homocysteine indicates poor absorption of vitamin B_{12} and folic acid, both important for cognitive function. Elevated plasma homocysteine also suggests an increased risk of vascular disease. Folate is particularly important for the proper development of the central nervous system and[305] folate deficiency may precede the development of Alzheimer's disease and vascular dementia.[306]

High-dose vitamin supplementation reduces homocysteine levels in patients with Alzheimer's disease. It's important to avoid folic acid, however, which is associated with cognitive decline because, as we age, we are not able to reduce it in its synthetic form to folate, the active form of folic acid. This leaves high levels of circulating folic acid in the body that may block folate receptors. When we are younger, this is not a problem, but it becomes progressively more difficult to process in synthetic form.[307] The appropriate form of folic acid to take is folate in capsule form or folinic acid, the injectible form of this vitamin.

High dose vitamin supplementation reduces homocysteine levels in patients with Alzheimer's

disease. They used B_{12}, folic acid, and B vitamins for 8 weeks.[308]

Antioxidant Benefits of Vitamins C and E

Vitamin E appears to slow the progression of Alzheimer's disease in some studies and to increase the lifespan of those taking it.[309–311]

In a study conducted by the Johns Hopkins University Bloomberg School of Public Health involving more than 4,700 Utah residents, results showed that supplementation with vitamin C and vitamin E reduced the prevalence of Alzheimer's disease.

Those taking vitamins C and E were 78% less likely to have a diagnosis of Alzheimer's disease at the start of the study, according to the researchers, and 64% less likely to have it four years later at its conclusion.[312–314]

Using these antioxidants may be a powerful risk lowering strategy by reducing the level of inflammation in the body and the amount of amyloid beta protein in the brain. In addition to supplementation, eating foods high in vitamin E, such as avocados and walnuts, may reduce the risk of Alzheimer's, most particularly among those with the genetic risk associated with the APOe (epsi) 4 allele.[315–331]

Powerful Botanicals to Help

Ginkgo Biloba

Ginkgo biloba is a known as a powerful vasodilator that helps with recall, mental focus, and cerebral functioning. It is an herb used in many treatments for energy and vascular function.

When combined with L-arginine and magnesium in one study, patients demonstrated a small improvement in their MMSE and a slowing of the progression of Alzheimer's disease.[332] It is generally well tolerated and produces good results.[333]

One study found that, when the effects of ginkgo and donepezil were compared in a twenty-four-week study, taking 160 mg of ginkgo was comparable to taking 5 mg of donepezil a day. The study involved 76 participants with mild to moderate Alzheimer's disease.[334]

Another study comparing the efficacy of 240 mg of ginkgo and 5 mg donepzil showed similar results.[335–337]

It's also useful in reducing oxidative damage, one of the earliest changes to occur in the development of these diseases.[338–343] Ginkgo appears to reduce amyloid beta deposition in the brain and its ability to cause neuronal cell death by lowering levels of LDL cholesterol without affecting the function of HDL cholesterol. This is important because high cholesterol levels appear to induce the production of amyloid beta in the brain.

Quercetin as a Protection from Oxidative Stress

Quercetin is a naturally occurring compound in many fruits and vegetables, notably onions and apples. One of its actions in the body is to stop degranulation of mast cells in the body, stopping them from releasing histamine and creating allergic symptoms. It's also been recently identified as an energy support.

It may provide protection from neurodegenerative changes in the brain, according to a Cornell University study. Brain cells from rats were exposed to both vitamin C and quercetin from apples, and then exposed to a source of hydrogen peroxide to replicate brain changes found in Alzheimer's disease. Those cells exposed to quercetin did the best, showing the least amount of damage when compared to vitamin C protected cells and those without exposure to antioxidants.[344]

8

What We Know Reduces Risk: Recent Research

Cancer History

In a recent reexamination of data from the Framington Heart Study, it appears that those who are survivors of non-skin cancers have a reduced risk of Alzheimer's disease, a benefit that is still present ten years after diagnosis. Part of this reduced risk, also observed in Parkinson's disease, may be linked to a specific gene that is activated in cancer but not functional in Alzheimer's disease.

Researchers also discovered that, in those with Alzheimer's disease, there is a reduced risk of having cancer. These two findings imply that cancer

and neurodegeneration are linked. What is most unusual is the negative correlation between the two diseases, cancer and Alzheimer's disease, with one disease conferring a protective benefit on the development of another disease.[345,346]

NSAIDs

As inflammation modulators, NSAIDs are being considered as therapy in those at risk for Alzheimer's disease. Their use is controversial, since clinical studies have not yet been done to demonstrate benefit.[347]

Research suggests that NSAIDs should be administered in the early stages of disease development to forestall the development of symptoms. To determine whether this would be effective would mean doing a prevention trial in cognitively normal individuals. Looking at epidemiological data, this could offer up to 58% protection on average. When examining the evolving social burden of Alzheimer's disease, treatment with NSAIDS may offer a low-cost, effective strategy to reduce the number of those afflicted with it.[348]

In particular, NSAID use may be most helpful in those who carry the APOE e4 allele, which dramatically increases risk of developing Alzheimer's, perhaps best applied during the early stages when amyloid beta deposits are occurring.[349,350]

9

Natural Therapies—What to Do if Cognitive Decline is a Problem

Improvement and Enhancement versus Therapy and Cure

IF YOU HAVE THE symptoms of cognitive decline, or they are already recognized and diagnosed, where do you begin? What is the difference between improvement and enhancement versus therapy and cure?

Currently there is no cure for dementia and Alzheimer's disease, though there are strategies that can help delay or alleviate the symptoms.

Conventional doctors will want to prescribe an anticholinesterase inhibitor, such as donepezil (Aricept®), to slow symptom development. Side

effects of administration of donepezil may include dizziness, muscle cramping, depression, insomnia, and GI symptoms such as nausea and vomiting. Many are not able to tolerate it very long.

There are some natural therapies to try, however, that have demonstrated some benefit in preventing cognitive decline.

Cognitive Training—Use Your Brain to Protect Your Brain

Studies show some evidence that "learning therapy" or cognitive training is helpful for those with Alzheimer's disease or vascular dementia. These types of programs involve creative, sensory, and mental stimulation processes to improve mental functioning and enhance abilities.

Cognitive stimulation therapy (CST) is one program designed for those with mild to moderate Alzheimer's disease and consists of fourteen sessions of themed activities. Results of studies showed a definite benefit in those who had received CST when compared to those who had not received stimulation. Benefits were estimated to be comparable to those achieved through medication and were cost effective.[351,352]

In a Japanese study of learning therapy, researchers found that memory was expanded when participants did a combination of activities that included arithmetic and storytelling. Participants

performed these activities for no more than fifteen minutes a day for three-to-five days a week. The mean age of participants in the study was eighty years of age.

In a similar US study, learning therapy improved Mini-Mental Status Exam (MMSE) results in those who participated in the therapy when compared to those who did not.[353,354]

Though their numbers are small, many other studies have shown similar results and there is now a call to provide these types of cognitive stimulation programs more widely for those patients with mild to moderate dementia.

Chicago Health and Aging Project (CHAP)

The Chicago Health and Aging Project was an educational and nutritional program designed to see if caregivers of patients with Alzheimer's disease could have a positive effect on patient weight and cognitive function. Malnutrition and weight loss are problems experienced by elders that are predictive of mortality and a decreased quality of life. The goal of the program was to determine if a specific educational program would help reverse this trend. Results of the program showed that the percentage of weight loss was decreased and scores on the MMSE improved in those patients who do not lose weight.[355]

Programs like this may be beneficial in those already diagnosed with dementia or Alzheimer's disease and may be available in many communities in the United States.

Controlling Hypertension and Diabetes

Oxidative stress is an important factor in the development of cognitive decline in many individuals. Controlling blood pressure and blood sugar are important strategies for reducing stress on the body that can increase mortality and progression to more severe stages of dementia.

Benfotiamine

Benfotiamine is a fat-soluble manmade form of vitamin B_1 used to prevent complications of diabetes. It's more commonly used in Europe in a range of 150–450 mg per day to protect blood vessels from damage caused by blood sugar elevations.[356]

Dietary Intake of Flavonoids

A high intake of flavonoids in the diet is associated with better cognitive function and maintenance of function over the course of ten years, according to one long-term French study. More than 1,600 people were assessed four times over the course of a decade and results showed that

those individuals with the highest intake of flavonoids maintained cognitive function better than those with the lowest intake.

Participants in the study were asked to indicate their intake of foods that included citrus fruit, kiwi, dried fruit, cabbage, spinach, French beans, asparagus, sweet pepper, oat flakes, chocolate, tea, coffee, soup, and fruit juice. The flavonoids isolated from foods included five major categories: quercetin, kaempferol, myricetin, luteolin, and apigenin. High intake of flavonoids and polyphenols appeared to be associated with reduced risk of conditions such as cardiovascular disease, asthma, and cancer, and could be a factor in preventing cognitive decline.[357]

Anodyne Therapy

Anodyne therapy is a portable form of light therapy that can increase nitrous oxide in the body, helping to restore damaged blood vessels, improve circulation, and provide pain relief. Scientifically, this type of therapy is known as monochromatic infrared photo energy (MIRE). It's a form of therapy often accompanying physical therapy sessions. While it is not curative, its effects last up to two days after therapy.

Anodyne therapy is helpful in restoring coordination, balance, and motor function in patients with spinal and nerve disorders, Alzheimer's

and Parkinson's disease, and other brain related conditions.[358]

Ayurvedic Herbs

Ashwaganda Extract

Ayurvedic medicine is the form of medicine that evolved in India. Many herbs within the Ayurvedic system are very helpful in the treatment of Alzheimer's disease.[359,360]

The Ayurvedic herb, Ashwaganda, also known as Withania somnifera, has many actions in the body that are similar to those of ginseng. It is an anti-inflammatory and tonifying herb known to support energy and the immune system. The active constituents, known as withanolides, have been used in India to support mental function in elders.[361]

The active constituents of Ashwaganda have shown the ability to support neuronal connections and in some cases, restore damaged connections, in animal studies. One study found that it may do this by increasing the receptors associated with acetylcholine and cholinergic function.

Ferulic Acid

Ferulic acid is a phenolic compound not unlike curcumin in its structure. It's found in many foods, such as oats, rice, wheat, coffee, peanuts, oranges, and pineapple. It's a strong antioxidant and anti-inflammatory that can protect neurons

against the damage caused by amyloid beta and inhibit its formation. Encouraging results have been observed in animal studies.[362]

Myricetin

Myricetin is a flavonoid found in many fruits and vegetables with known antioxidant and anti-inflammatory properties. It appears to be beneficial in reducing glutamate excitotoxicity by modulating the NMDA receptor, reducing intracellular calcium overload, and limiting oxidative damage due to reactive oxygen species (ROS). All of these actions help to reduce neuronal damage and cognitive decline.[363]

Minerals

Lithium

Studies have shown that lithium may inhibit the formation of amyloid beta plaque. Once it has been formed, lithium may help prevent neuronal degradation and damage from occurring which can lead to cognitive decline.[364]

Lithium aspartate or lithium orotate used in small doses may help prevent abnormal brain aging.

Niacin and Niacinamide

Low intake of niacin (vitamin B_3) has been associated in some studies with a higher risk of Alzheimer's disease.

In a study conducted by Chicago's Rush Institute for Healthy Aging, consuming high levels of dietary niacin may reduce the risk of cognitive decline. Niacin is found in highest amounts in high-protein foods, including beef liver, chicken, tuna, salmon, and peanuts.

Niacinamide, also known as nicotinamide, is a type of vitamin B_3 that has shown very promising results for the reversal of Alzheimer's disease in an animal study conducted at the University of California, Irvine. Niacinamide, which can cross the blood-brain barrier, reduced tau protein levels in the brains of animals by up to 60%. This is remarkable, since tau protein is usually high in Alzheimer's disease. Many of the animals reportedly functioned as if they had never experienced cognitive decline, according to study authors. Though this has not yet been studied in human subjects, it is a very exciting finding.[365]

Supplemental niacinamide can be purchased in 500 and 1000 mg capsules. It's important to monitor liver function when taking niacinamide in higher doses. It's advisable to work with a physician skilled and knowledgeable in the use of natural supplements for best results.

Galantamine

Galantamine is a natural alkaloid reported to increase the neurotransmitter acetylcholine.

Galantamine comes from the plant Galanthus nivalis also known as the common snowdrop. Evidence suggests that it can delay the progression of dementia by as much as 18 months by increasing cognition. While it is not a cure, it is at least as effective as the patent medications.[366]

Galantamine has several distinct modes of action in the brain. It acts like an acetylcholinesterase inhibitor, it accentuates the effects of acetylcholine in the brain through its stimulation of nicotinic receptors, and it increases acetylcholine while supporting other neurotransmitters like GABA and serotonin.[367] Clinical trials have observed that the patient's condition improves for several months, with benefits lasting up to twelve months. Galantamine is well tolerated without significant adverse effects.

An over the counter capsule working on the same principle is available as Galantamind.

Botanicals and Plant Constituents

Much of the conventional approach using drug therapies has focused on fixing the neurotransmitter defect involving acetylcholine, which is required for short-term memory. These approaches have involved trying to develop acetylcholine precursors, agents that turn on or turn off different receptors, and those agents that inhibit enzymes involved in the pathway. These

have included muscarinic agonists, nicotinic agonists, and acetylcholinesterase inhibitors. While some drugs have been approved, not all of the outcomes have been satisfactory and there remains a very big opportunity to use alternative medicines, including botanicals, as therapy.[368,369]

American Ginseng

Animal studies have shown that American ginseng, also known by its Latin name, Panax quinquefolius, may reduce neuronal cell death and have protective properties against Alzheimer's disease. Many believe that using ginseng regularly may protect against cognitive decline.

In experimental studies, ginseng had a positive effect on memory in those with Alzheimer's disease and this improvement was assessed and monitored with the Mini-Mental Status Exam (MMSE) and the Alzheimer's disease assessment scale (ADAS).

The study ran for twelve weeks and, when ginseng was discontinued, improvement declined to that of the control group that had not been taking ginseng. It seems to be a clear indication of benefit in protecting memory and mental function in those with Alzheimer's disease.[370]

Ginseng may be used safely by most people, though it should not be used by those with diabetes. It should not be used in pregnancy, schizophrenia, or in those with disturbed sleep.[371]

The usefulness of another type of ginseng, Korean Red Ginseng, has also been studied using different doses of the botanical medicine. Those using the highest amounts of the Korean red ginseng showed the greatest improvement during the twelve-week study.[372]

Subsequent studies of ginseng have not shown as dramatic improvement as some of the earlier studies and some researchers believe results are inconclusive to date on the benefits of ginseng in the treatment of Alzheimer's disease. Further assessment is indicated; in other words, the jury is still out on the potential benefits of ginseng in any neuroprotective program.[373,374]

Bacopa

Bacopa monniera is an Ayurvedic herb that has been used traditionally to reduce chronic stress and promote memory and mental ability. This herb may be useful in the treatment of Alzheimer's disease by reducing the accumulation of amyloid beta plaque in the brain.

In animal studies using bacopa and ginkgo biloba, acetylcholinesterase was inhibited in mice, showing potential benefit in the treatment of Alzheimer's disease.[375,376]

Gotu Kola

Centella asiatica, known more commonly as gotu kola, is an herb used extensively in the Ayurvedic

system of medicine that developed in India. A number of studies have indicated its memory enhancing abilities in animal studies. It has a stimulating effect on neuronal dendrites in the hippocampus and seems to improve memory through increased cellular mechanisms that have an effect on amyloid beta.[377]

Green Tea

Green tea has many positive effects in the body and is used to treat many conditions, including breast cancer and reducing oxidative stress in the body. As oxidative stress has been implicated in brain senescence and loss of cognitive function, the polyphenols contained in green tea may prevent memory regression and the damage to DNA caused by oxidative stress. Daily consumption of organic green tea is recommended and up to ten cups a day is helpful. Organic tea contains the constituent, epigallocatechin-3-gallate (EGCG), which is needed to reduce oxidative stress, whereas processed tea has this important principle removed since it is bitter. Despite the taste, bitter is better.

Green tea appears in studies to protect against neuronal degeneration. In rodent studies, animals showed decreased neuronal degeneration in the hippocamal area of the brain while on green tea supplementation. This type of neuronal degradation is also seen in patients with Alzheimer's disease.[378]

Green tea extract also regenerated nerve cells in mice and prevented additional damage in an animal study. The dose equivalent to that given the animals was between 1500 and 1600 mg a day, a dose already found safe for human consumption in previous studies.[379]

Huperzine A

Huperzine A is an alkaloid extract obtained from the Chinese club moss, Huperzia serrata, believed to improve cognitive and intellectual performance in patients with mild cognitive impairment, dementia, and Alzheimer's disease. It may also be of benefit in healthy individuals, holding off age-related and other neurodegenerative changes. It appears to protect neurons from oxidative stress caused by amyloid beta.

Huperzine A has been used as a therapy in traditional Chinese medicine for centuries. It is a very potent inhibitor of the enzyme, acethycholinesterase, which breaks down the neurotransmitter, acetylcholine, in the brain. Acetylcholine decrease in the brain is associated with memory loss. If huperzine could maintain higher levels of acetylcholine in the brain, it might be of benefit in reducing progression of cognitive impairment.

Human trials have been conducted with promising results. In one investigation using 103 subjects, 60% showed some degree of improvement in cognitive function. Similar results have been

obtained in other studies. However, not all the evidence is conclusive and not all results have been as favorable.

Huperzine A is a potent herbal extract with effects that have been compared to those of galantamine, a drug used in the treatment of Alzheimer's disease. Since it is more like a drug than an herb, it should be used cautiously. In supplement form, doses from 100–200 mcg twice a day have been used for age-related memory loss. It has not been tested under all health conditions and should not be used by those who are pregnant, or who have liver or kidney disease unless under a doctor's guidance.[380]

Lion's Mane

Lion's mane, also known as Hericium erinaceus, is a type of mushroom containing compounds known as hericenones and erinacines that are reported to stimulate nerve growth factor (NGF), a protein that repairs neurons in the brain. One study has shown that this mushroom improves the mind and increases the ability of patients with dementia to walk, eat and dress themselves. It works by increasing acetylcholine levels in the brain, the neurotransmitter that is important to maintaining memory and learning. The average dose of dried lion's mane used in the study was 5 grams, provided in a soup over the course of six months. A recommended dose of Lion's Mane

is four capsules a day, with results taking a minimum of six months. Anyone with a mushroom allergy should not take this product.

Other mushrooms or nutrients that have been used along with lion's mane are Maitake (D-fraction), a mushroom with known to enhance immune function; Reishi, a strong anti-inflammatory; and vitamin C, an antioxidant.

Another study conducted in Japan showed that lion's mane improved mild cognitive impairment among study subjects.[381,382]

Oleocanthal to Prevent, Treat Alzheimer's Disease

Oleocanthal is a naturally occurring compound in extra-virgin olive oil that may help improve damaged brain cells in dementia and Alzheimer's disease. From recent studies, this compound is believed to bind to the toxic proteins causing damage in the brain—beta amyloid oligomers—and prevent them from having an effect. Oleocanthal also made the toxic proteins more attractive to antibodies, increasing the immune response. This suggests a possible type of immunological treatment for the future.[383]

The compound, oleocanthal, has also been found to have anti-inflammatory properties, similar to those found in ibuprofen. Although chemically very different, the two may share similar effects on the anti-inflammatory pathway to the

prostaglandins. There is evidence that NSAIDs like ibuprofen may have a risk-reducing effect on Alzheimer's disease, suggesting even more ways that olive oil may be of benefit.[384]

Pomegranate

Researchers at Loma Linda University in California have discovered that pomegranate juice has the potential to decrease the level of amyloid beta in the brain and increase cognitive function, according to results from an animal study. When animals were given pomegranate juice from six to thirteen months of age, they showed reduced amyloid plaque accumulation in the brain. Animals that were juice fed demonstrated a better ability to navigate a water maze than animals in the control group not receiving pomegranate juice.

Pomegranate is also believed to reduce inflammation from osteoarthritis, prevent endothelial dysfunction associated with cardiovascular disease, and promote healthy blood pressure and blood sugar levels.[385]

Resveratrol

Resveratrol is a naturally derived compound known as a polyphenol found in pomegranate, grapes, and red wine that has received a great deal of press lately about its anti-aging properties. It

may have the ability to degrade amyloid plaque buildup in Alzheimer's disease according to some researchers.[386,387]

One of the ways it may help reduce the risk factors associated with dementia is through its cardioprotective benefits. Dementia risk is reduced by protecting cardiovascular health and vascular integrity.

Calorie restriction and resveratrol appear to have similar protective benefits for the aging heart.[388,389]

Rhodiola Rosea

Rhodiola rosea is an herb first discovered in Russia where it has been used by traditional healers to treat depression, reduce stress, and improve energy. Current research suggests it may be a promising anti-aging herb, since it has shown the ability to slow the aging process of animals in research studies, thereby increasing the lifespan.

Its benefit may just come from its ability as an adrenal adaptogen to slow down and even out the adrenal gland's output of cortisol, providing the body with enough for the day at an even pace. This could be of benefit in the prevention of dementia and Alzheimer's disease, which increase in incidence as we age and as the amount of cortisol increases in the body over time. It is beneficial in increasing mental alertness and endurance, decreasing anxiety, reducing migraines, and helping with sleep.

It is not recommended in individuals with bipolar disorder, during pregnancy, or anyone with a known allergy to it.[390,391]

Rosemary Extract

The herb, Rosmarinus officinalis, is a commonly used kitchen herb. It also contains the active ingredient, carnosic acid, which may have neuroprotective benefit. In studies, it seems to activate a specific pathway that protects neurons from oxidative stress and excitotoxicity. The pathway that it supports reduces damage caused by reactive oxygen species (ROS), one of the risk factors in the development of cognitive dysfunction.

Interestingly, carnosic acid is an example of a "pathological-activated therapeutic" or "PAT" that only activates when free radical damage is present and does not otherwise do anything when not needed. It's a naturally occurring therapeutic that is very safe and well tolerated. The constituent of rosemary, 1, 8-cineole, may enhance individual results on mental stimulation testing and may influence mood. When healthy volunteers were allowed to inhale the aroma of rosemary containing this constituent, they performed more quickly and more accurately than in testing prior to exposure to the aroma. Participants in the study were not told that they were being assessed for their responses when exposed to the aroma of rosemary for random periods of time ranging from

four to ten minutes. Test responses increased as the concentration of 1,8-cineole absorbed in the blood increased, showing that higher concentrations of the rosemary worked more effectively.

These results have important implications in the area of dementia management and prevention. Traditional medicine has long been aware of the effect of essential oils on memory and mood. The compound, 1,8-cineole, is an acetylcholinesterase inhibitor, the enzyme that is the most common target of Alzheimer's drug therapy. It is only moderately effective in this capacity and, when combined with other compounds like alpha-pinene and beta pinene, which act similarly, demonstrates a greater degree of inhibition of cholinesterase.[392]

Rosemary has many known therapeutic benefits, including serving as a mild diuretic in cases of edema, improving kidney function, and acting as a detoxifier, possibly by increasing glutathione levels. Used in cooking or in supplements, it may have protective benefit in any program designed to reduce risks of developing cognitive impairment.[393,394]

Salvia Officinalis

There are two herbs with similar properties that have shown improvement in memory in clinical studies. The first is sage, or Salvia officinalis, a popular kitchen herb that has been used for centuries

as a botanical medicine. When sage is used daily, it may help with memory and cognitive function. A study in the Journal of Clinical Pharmacy and Therapeutics reported this as a possible treatment that also reduced agitation, attention, and behavior, common problems in patients with Alzheimer's disease.[395]

Similar effects have been noted using the Spanish sage, S. lavandulaefolia. It acts primarily as an inhibitor of the enzyme, acetylcholinesterase.[396,397]

Melissa officinalis, also known as lemon balm, has similar properties as sage and appears to support memory and reduce agitation in patients.[398]

An important side benefit is its ability to improve mood and thus, quality of life. In a recent study, 60 drops of lemon balm were used in patients with mild to moderate Alzheimer's disease. When the results were tabulated, there was a significant improvement in cognitive function when compared to placebo and it had a positive effect on agitation.[399]

Silicic Acid

For many years, aluminum has been suspected as a causative agent for Alzheimer's disease, along with other metals, since it has been found in the neurofibrillary plaque and tangles in the brains of those affected with the disease. Some have reported finding links between the development and progression of the disease and levels of exposure to it,

though we do not know whether the relationship is causal or accidental. We are exposed to aluminum daily, mostly from food and water, along with other elements including iron, copper, zinc, and fluoride, any or all of which could have a modifying effect on toxic mineral levels.

Aluminim is a known neurotoxin and anything that might remove it from the body could be useful as a therapeutic agent. Researchers have proposed using silicic acid, or silicon, as a non-invasive agent to remove aluminum from the body, since it reduces oral absorption and helps remove it through the urine. It is not certain, however, if this treatment is useful or effective and what dose, if any, might be needed to reduce toxic levels. Research is still uncertain about the role aluminum plays in the development of Alzheimer's disease and other dementias and more studies are needed to clarify this.[400–403]

Uncaria Rhynchophylla

Uncaria rynchophylla, or Cat's Claw, is an herb used commonly in Chinese medicine that has sedative actions and is often used to treat epilepsy, ADD/ADHD, ulcers, and gastritis. It may be a useful herb to include in any strategy aimed at inhibiting the formation of amyloid beta in the brain since it has a potent inhibitory effect. Cat's Claw could be a novel therapeutic agent in the treatment of dementia and Alzheimer's disease.[404,405]

Vinpocetine

Vinpocetine, derived from the plant known as lesser periwinkle, is often given as a prescription medicine in Europe and Asia to increase oxygen transport to the brain.

In an experimental animal model of dementia, researchers induced neurodegenerative lesions in rats then administered vinpocetine intraperitoneally. Those rats not receiving vinpocetine did poorly when they were subjected to behavioral testing, including their ability to recognize new objects and other rats, and their ability to move through the Morris water maze. In rats that received vinpocetine, these behavior deficits were reduced. Researchers also noted that learning disabilitites and attention deficit was alleviated in the rats.[406]

In another study, vinpocetine protected astrocytes from low oxygen levels in vitro. When vinpocetine was administered to cell cultures, the number of dead cells was dramatically reduced under low oxygen, or hypoxic, situations. It also improved mitochondrial function and increased the level of ATP, very important in overcoming mitochondrial deficit. Researchers concluded that vinpocetine was protective of astrocytes, at least in test tube studies.[407]

Sea and Other Naturally Derived Sources

Aequorin

The jellyfish, Aequorin victoria, is reported to prevent calcium dysregulation and could be of use in the treatment of Alzheimer's disease, according to one researcher. It's being studied because of its ability to keep brain cells alive longer in experiments done with laboratory animals and correct for calcium imbalance in those cells, which commonly occurs in this disease. According to researchers, the jellyfish is not harmed in the process of extracting its important constituents. [408,409]

In a recent study entitled the "Madison Memory Study," this jellyfish extract was given to 218 adults over the course of ninety days and improved word recall, short-term memory and overall execution of mental function as compared to placebo. Those involved in developing this compound recommend daily use to improve cognitive function.[410]

Coconut Oil

Coconut oil is a saturated fat that provides high levels of medium-chain triglycerides to the body and increases the ketone, beta-hydroxybutyrate. Increased memory and recall were associated with higher levels of this ketone provided through supplementation with coconut oil in a study[411] involving adults with cognitive impairment.

An advantage of coconut oil is that it does not oxidize, thus avoiding problems associated with oxidation that can increase dementia risk. No known level of intake has been established for coconut oil.

Fish Oil

The Mediterranean diet, which is high in healthy oils and omega-3 fatty acids, was shown to lower risk of Alzheimer's disease by 19–24% when participants stayed on the diet, researchers at Columbia University Medical Center concluded. The lead investigator speculated that the mechanism of action may be due, in part, to its anti-inflammatory effects.[412]

Research has shown that the component of fish oil, DHA, boosts brain function and improves cardiovascular health by supporting the structural integrity of the membranes of brain cells.[413]

In a related study, researchers demonstrated that omega-3 fatty acids could relieve depression and agitation in patients with Alzheimer's disease.[414,415]

A high intake of omega-6 fatty acids, more commonly associated with the American diet, with a low intake of omega-3 fatty acids, may double the risk of developing Alzheimer's disease and dementia.[416]

Supplements

Acetyl-l-carnitine, R-lipoic acid, and CoQ10 are potent energy producers in the body and support mitochondrial function.

Acetyl-L-Carnitine

Carnitine is a nutrient that is important to the functioning of astrocytes, a type of star-shaped glial cell found in the brain. L-carnitine is an amino acid derivative that is needed to transport fatty acids into the mitochondria for energy production and to transport toxic compounds out of the cell. Acetyl-L-carnitine is the supplemental form of L-carnitine that is best for oral use since it is absorbed more effectively. Acetyl-L-carnitine protects neurons and acts as an antioxidant in the mitochondria in the body and in the brain.

It may help those already diagnosed with Alzheimer's disease by improving cognitive function and slowing down the progress of the disease. It may be that those with Alzheimer's disease have less L-carnitine than others, predisposing them to mitochondrial dysfunction.

Acetyl-L-carnitine has also been used to improve the efficiency of donepezil therapy in the treatment of Alzheimer's disease because of its antioxidant properties.[417,418]

Lipoic Acid

The coenzyme, lipoic acid, is a compound found in the mitochondria and necessary for energy production in the electron transport chain. It may help in the early stages of Alzheimer's disease and dementia because it increases ATP production and may be significant in conditions of energy deficit. In the case of dementia, it is known to activate the enzyme that facilitates acetylcholine production in the body. As a potent antioxidant, it reduces inflammation in the body and increases the availability of glucose for use by brain cells.[419]

The most biologically available form of lipoic acid is R-alpha-lipoic acid (also known as thioctic acid); studies have shown that use of this compound improves mitochondrial energy production and reduces damage from oxidative stress. It's been used to reduce neuropathy and improve nerve conduction in those with diabetes without major side effects.

When acetyl-L-carnitine and R-lipoic acid were fed to animals in one study, they reduced oxidative damage in the hippocampus of older animals and restored mitochondrial function to levels commonly seen in much younger animals. Mitochondrial dysfunction is often associated with Alzheimer's disease and any combination of compounds able to cross the blood-brain barrier and improve memory and energy deficit is a potentially valuable form of supplementation.[420,421]

It is also known to chelate iron, reducing toxic levels in the body.

CoQ10

Oxidative stress is one of the proposed causes of Alzheimer's disease because it increases free radicals that can damage tissue and organs. The antioxidant, Coenzyme Q10, also known as CoQ10, plays a big role in the electron transport chain by quenching free radical production and supporting energy production. It reduces oxidative stress as a result and increases the levels of adenosine triphosphate (ATP), which increases energy produced by the mitochondria, the cellular powerhouse. It's found in the highest amounts in the liver, heart, kidney, and brain.

In an animal model, supplementation with CoQ10 improved cognitive performance and reduce levels of amyloid beta and plaque accumulation. Those animals not receiving this supplement did not achieve the same level of cognitive function and studies of their brains revealed structural changes consistent with neurodegeneration.

Human trials have shown that supplementaton with CoQ10 is safe, though specific use in Alzheimer's disease has not yet been established. CoQ10 is currently used in those taking statin medications, to delay the development of Parkinson's disease, in the treatment of congestive heart failure and can help reduce the frequency of migraines. The active

form of CoQ10, ubiquinol, is recommended since it is more biologically available to individuals and remains in the body longer.[422–424]

Choline and Phosphatidylcholine

Choline is an essential nutrient that synthesizes phospholipids that add integrity and strength to cell membranes. Choline is a precursor to the neurotransmitter, acetylcholine, which is often found in low amounts in the brains of those with Alzheimer's disease. In the body, choline is found as part of the fat or phospholipid molecule, phosphatidylcholine, or lecithin. Phosphatidylcholine is part of the cholesterol molecule, VLDL, or very low-density lipoprotein, and is necessary to transport fats needed by tissues through the body. When it is inadequate in the body, these deleterious fats can be deposited in the liver, where they are not needed.

Supplementation with choline and phosphatidylcholine may help support cell membranes that naturally degrade with age.

In that Alzheimer's disease involves neurodegradation, it makes sense to consider using choline as a cognitive support to repair neuronal membranes. In at least one study of 84 patients with memory loss varying from mild to moderate, using choline for six weeks improved their responses on the Mini-Mental Status Exam (MMSE) and improved learning skills.[425]

Studies for its use are still inconclusive, however, due to the small numbers included in many of the trials. Additional research continues on determining its effectiveness for use with dementia and Alzheimer's disease.[426]

The supplement, L-alpha glycerylphosphorylcholine (available as Alpha GPC), is a precursor to acetylcholine and a bioavailable form of choline that helps support brain function.

S-adenosyl-methionine (SAMe)

Investigators have identified a possible link between a deficiency in the naturally occurring compound, S-adenosyl-methionine (SAMe), and the risk of developing Alzheimer's disease. In a study of mice bred for increased genetic risk for Alzheimer's disease, the mice developed cognitive impairment when they were made deficient in folic acid, a B vitamin. SAMe is necessary in the body for a variety of reactions involving methyl donors that reduce oxidative damage in the body.

When the mice were supplemented with folic acid, then the neurodegenerative changes stopped. The deficiency of the methyl donor SAMe allowed the body to express too much of the protein, presenilin-1, which increased the production of amyloid beta, a compound toxic to the brain and associated with the pathophysiology of Alzheimer's.

By identifying this deficiency, researchers have found a link between nutritional deficiencies and

genetic risk, supporting supplementation to correct it. The researchers followed up and confirmed their findings in a second study.[427,428]

10

Effective Pharmacologic Therapies

THERE ARE A FEW therapies that exist that may be considered pharmacologic because they are not naturally occurring, and yet may be effective and not harmful.

Piracetam may be one of those agents, since it is classified as a drug but often viewed as a food supplement in Europe. It is a nootropic drug, often used to treat cognitive impairment in aging, brain injuries, and dementia. Nootropics, sometimes described as "smart drugs," have a positive effect on mental function at a very low dose.

Piracetam has been used for many years for cognitive impairment and it has shown some ability to enhance mitochondrial membranes in the

brain. In a meta-analysis of studies using piracetam for cognitive impairment, there is strong evidence for its effectiveness in older individuals.

With mitochondrial dysfunction a risk factor in the development of abnormal brain aging and dementia, its actions support ATP synthesis and prevent the degradation of cells. The positive spin that piracetam has added to treatments for dementia is from its ability to stimulate function at the level of the synapse and improve the "plasticity" of the brain. Increased plasticity allows neurons to develop new pathways to overcome deficits.[429]

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About the Author

Lauren Russel, ND, is a board-certified licensed Naturopathic Physician in full-time practice at Tahoma Clinic in Washington State. In her medical practice, she focuses on bio-identical hormone therapy for men and women, thyroid imbalances, adrenal fatigue and stress management, gastrointestinal and digestive health, food allergies, sleep issues and nutritional optimization. She was the lead researcher on two studies investigating the effects of physiologic doses of the hormone, aldosterone, on hearing loss in study volunteers at Tahoma Clinic.

She received her doctorate degree in Naturopathic Medicine from Bastyr University in Kenmore, Washington, and undergraduate degree in the Biological Sciences from the State University of New York at Stony Brook. Dr. Russel also serves as an adjunct to the naturopathic

medicine department at Bastyr University to facilitate key training and testing programs to improve the skills of medical students.

She has been a medical writer and editor for more than 25 years, working with several prominent, peer-reviewed medical and scientific publications and has developed continuing education materials for healthcare professionals throughout the United States.

She has been a contributing author to the publications, *NDNR: Naturopathic Doctor News and Review*, the *Townsend Review for Doctors and Patients*, and *Life Extension Magazine*. She has also co-authored articles with Dr. Jonathan Wright, MD, and researched topics for the newsletter, *Nutrition and Healing*.