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REPORT

Does Mild Cognitive Impairment Concern You?

Reducing the Danger of Silent Neurological Decline

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Conventional physicians have yet to recognize the growing epidemic of mild cognitive impairment that faces our aging population. Currently, there is no standard medical protocol for preventing or treating this condition that may be a precursor to Alzheimer's disease. In this article, physician Dr. Rosick discusses the need for early diagnosis and preventive treatment.

THE EPIDEMIC OF ALZHEIMER'S DISEASE

Clinically described in 1906, Alzheimer's is the most common cause of dementia in those aged 65 or older. It is characterized by a progressive decline in both cognition and memory. With the rapidly aging population in the United States, projections are that 20 million people in the United States will develop this extremely debilitating neurological disease during the next four decades.[1,2] However, there is another condition that all of us, elderly or not, need to be concerned about when it comes to suboptimal brain function—mild cognitive impairment.

IS MILD COGNITIVE IMPAIRMENT AN EARLY FORM OF ALZHEIMER'S DISEASE?

Who among us doesn't forget things now and then? As a busy physician practicing integrative medicine at a university medical center, I find that it's not unusual to forget even the simplest of things—like where I've left my car keys or what room my stethoscope is in (fortunately, I generally don't forget what room my patients are in!). In fact, I'm sure it's safe to say there is practically no one in our fast-paced, high-stress world who does not have these episodes of forgetfulness. For most of us, while annoying, these bouts of memory meltdown are not a big deal. But for some people—those who suffer from mild cognitive impairment—it is a potentially serious problem.

Mild cognitive impairment represents a process in which individuals show a statistically significant decline in their memory when compared with other patients of the same age and gender. In contrast to patients with Alzheimer's disease, people with mild cognitive impairment generally have no other cognitive complaints—that is, they have no problems driving, dressing themselves, cooking dinner, etc.

It should be noted that research into mild cognitive impairment is still new. In fact, there is no consensus among mainstream (or even integrative) physicians on what does and does not comprise mild cognitive impairment.

"If I have mild cognitive impairment, does that mean I'll automatically get Alzheimer's disease?" is a question I often hear, and the answer, at least from the data we currently have, is "no." Studies show that people with mild cognitive impairment do not automatically go on to develop Alzheimer's disease. In the 2004 Canadian Study of Health and Aging in 296 men and women, 29% remained stable—that is, they did not deteriorate further into Alzheimer's disease, while 10% recovered—that is, they regained normal memory and cognitive function.[3] In a more recent study published in 2007, Italian researchers examined 52 elderly men and women (average age of 73 years) with mild cognitive impairment over a period ranging from two months to three years. The researchers found that almost 54% of the patients remained stable in terms of their memory retention, while 17% of them regained normal brain function.[4]

"So even if I have mild cognitive impairment, are you saying that I don't have to worry about progressing to Alzheimer's disease?" is a reasonable question many of you are probably asking. Unfortunately, that's not the case. Preliminary data indicate that about 10% or so of people with mild cognitive impairment will go on to develop Alzheimer's disease versus only 2% of the general population. Because of this statistically increased risk, I believe it is imperative that we in the medical community—both mainstream and integrative—be aggressive in formalizing tests and standards to determine if a person is

developing mild cognitive impairment. Unfortunately, that day isn't here yet. Because subtle changes in memory and cognition happen to all of us at certain times—and especially as we age—defining who has mild cognitive impairment remains a critical challenge. New screening tests—such as the Montreal Cognitive Assessment—are being developed to provide health care providers with a rapid, sensitive tool to assess memory and mild cognitive impairment. In addition, imaging studies like magnetic resonance imaging (MRI) have shown that people with mild cognitive impairment, like those with Alzheimer's disease, tend to have a loss of cells in the hippocampus, an area of the brain that is critically important to memory formation.

PREVENTING MILD COGNITIVE IMPAIRMENT

Because people with mild cognitive impairment have a small but statistically increased risk of developing Alzheimer's disease, the American Academy of Neurology has recommended that people with suspected mild cognitive impairment should be monitored closely by a physician. Since it is known that early detection and treatment of Alzheimer's disease is important, it only makes sense to think that if you are at risk for mild cognitive impairment, the sooner you can take steps to prevent its progression, the better. As an anti-aging, holistically trained physician, the bottom line to me is recognizing whether or not mild cognitive impairment will lead to Alzheimer's disease and beginning a program that may very well delay—or even prevent—mild cognitive impairment, and therefore, Alzheimer's disease.

MILD COGNITIVE IMPAIRMENT AND ALZHEIMER'S DISEASE—COMMON CAUSES?

Because of some similarities between mild cognitive impairment and Alzheimer's disease, researchers have begun to examine whether these two disease states share common etiologies. Damage to brain cells through the excess production of free radicals may be a key process common to both mild cognitive impairment and Alzheimer's disease. Free radicals are molecules that are produced inside brain cells and every other cell in the body when energy is generated. However, in certain diseases like Alzheimer's, free radicals are produced in much greater amounts than normal. These excess free radicals are now known to cause significant damage to the brain that can lead to actual nerve cell destruction. An important review article reported that in the autopsied brains of patients with Alzheimer's disease, there were many hallmark pathological changes caused by free-radical activity, including DNA damage, protein oxidation, and lipid peroxidation.[5]

With the knowledge that free radicals are most likely involved in Alzheimer's, researchers are now examining whether or not these destructive biomolecules are involved in the genesis of mild cognitive impairment. A study published in Neurology showed that, in the authors' own words, ***"oxidative damage occurs in the brain of subjects with mild cognitive impairment."***[6] In an even more recent study published in 2007, researchers presented data showing that in patients with mild cognitive impairment, there was significant evidence of excess free-radical production and oxidative damage. In light of this evidence, the authors of the study concluded, ***" ..antioxidants or combinations of antioxidants are necessary to decrease oxidative damage in mild cognitive impairment and Alzheimer's."***[7]

Finally, another recent study examined the blood levels of numerous antioxidants—including vitamins A, C, and E along with lutein and zeaxanthin—in the plasma of both male and female patients with mild cognitive impairment, Alzheimer's disease, and healthy control patients. The study unequivocally showed that both the level and biochemical activity of all these antioxidants were lower in patients with both mild cognitive impairment and Alzheimer's. Because of this, the authors stated in no uncertain terms, "as mild cognitive impairment may represent a prodromal stage of Alzheimer's disease, and oxidative damage appears to occur as one of the earliest patho-physiological events in Alzheimer's disease, ***an increased intake of antioxidants in patients with mild cognitive impairment could be helpful in lowering the risk of conversion to dementia.***"[8]

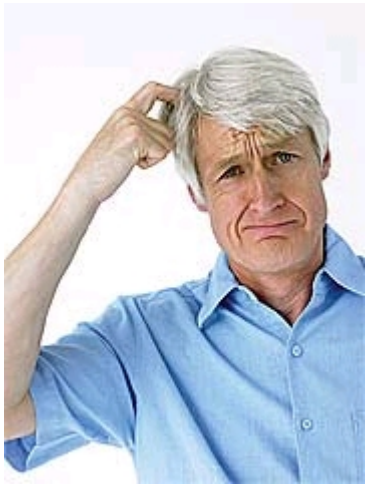
USING ANTIOXIDANTS TO PREVENT MILD COGNITIVE IMPAIRMENT AND ALZHEIMER'S DISEASE

With the knowledge that oxidative damage to brain cells may be part of the process that leads to both Alzheimer's disease and mild cognitive impairment, it makes sense to think that antioxidant supplements could be important weapons in the war on these forms of dementia that lead to cognitive and memory changes. One early study that examined 442 elderly patients in Basel, Switzerland, found a direct correlation between the blood levels of two common antioxidants (beta-carotene and vitamin C) and memory retention.[9] Another study reported on the reduced risk of Alzheimer's in people who took antioxidant supplements. The results of the study should come as no surprise, and unequivocally showed that, in the authors' own words, "use of vitamin E and vitamin C supplements in combination is associated with reduced prevalence and incidence of Alzheimer's disease. Antioxidant supplements merit further study as agents in the primary prevention of Alzheimer's disease."[10] What we are learning, however, is that traditional antioxidants like alpha-tocopherol vitamin E may not be enough to protect neurons against free radicals in the long

run.

RESVERATROL—A NATURAL ANTIOXIDANT VITAL FOR PREVENTING MILD COGNITIVE IMPAIRMENT

A useful antioxidant in preventing mild cognitive impairment and Alzheimer's disease may be found in an age-old drink—red wine. Resveratrol is a poly-phenol found primarily in the skin of grapes, and it is present in significant amounts in red wine.



Multiple studies demonstrate the significant beneficial effect that resveratrol has in protecting brain cells from the ravages of free radicals. One published study examined the protective effect of black grape skin extracts (which are high in resveratrol) on cellular toxicity produced by the beta-amyloid peptide in human endothelial cells.[11] The researchers showed, that, at least in the laboratory setting, the grape skin extract reduced free-radical production by beta-amyloid (a pathological protein often found in the brains of Alzheimer's patients), along with protecting the epithelial cells' membranes against free-radical induced damage.

Two other studies have lent credence to the idea that resveratrol can provide protection against Alzheimer's disease and mild cognitive impairment through its antioxidant activity. One study examined the effects of resveratrol on human neuroblastoma cells subjected to oxidative stress generated from damaging beta-amyloid peptide.[12] Resveratrol was effective in restoring glutathione (an intracellular free-radical scavenger) levels in the human cells that were subjected to beta-amyloid. Another published study showed that resveratrol protected cultured rat cells against beta-amyloid-induced cytotoxicity and intracellular accumulation of free radicals.[13]

WHAT YOU NEED TO KNOW: ARE YOU AT RISK FOR MILD COGNITIVE IMPAIRMENT?

- One of the most serious and debilitating illnesses facing aging adults is Alzheimer's disease. Alzheimer's leads to progressive and irreversible memory loss and dementia.
- Medical science is increasingly recognizing a milder form of memory loss termed mild
- cognitive impairment. Individuals with mild cognitive impairment show decline in memory function when compared with healthy patients of the same age.
- People with mild cognitive impairment face a slightly higher risk of developing Alzheimer's; aggressive prevention strategies are therefore warranted to help avert both these ominous conditions.
- Free radical-induced damage to brain cells has been implicated in both mild cognitive impairment and Alzheimer's.
- Antioxidant-boosting nutrients such as glutathione, resveratrol, lipoic acid, acetyl-L-carnitine, and SAMe show promise in offsetting the pathological changes associated with mild cognitive impairment and Alzheimer's.
- Another key brain nutrient called phosphatidylserine has been found in clinical trials to help preserve memory function with aging.

GLUTATHIONE: FIGHTING FREE RADICALS AND PROTECTING AGAINST MILD COGNITIVE IMPAIRMENT

Glutathione is one of the most effective free-radical fighters in the human body. With the knowledge that both Alzheimer's disease and mild cognitive impairment are associated with an excess of free radicals, maintaining optimal glutathione levels may be critical in preventing these diseases. A review article in the journal Archives of Biochemistry and Biophysics discussed both the decline of glutathione in the heart and brain, along with the vital importance of optimal gluta-thione levels.[14] As the authors state, "a heightened pro-oxidant cellular environment is particularly evident in metabolically active tissues, such as the heart and brain; in turn, these organs are prone to develop life-threatening pathophysiological conditions such as congestive heart failure and Alzheimer's disease… the brain and the heart are especially vulnerable to oxidative insult owing to their relatively limited glutathione-dependent antioxidant activity."

For those in mainstream medicine who continue to doubt the importance of glutathione in maintaining cognitive abilities, a recent article in the prestigious Annals of the New York Academy of Sciences should quash their skepticism.[15] In an elegant series of experiments, scientists compared blood glutathione concentrations between female and male patients with Alzheimer's disease

and age-matched controls. Researchers found that glutathione content was not significantly different among women with Alzheimer's and those without the disease. In men, there was a substantial decrease in glutathione concentrations in the red blood cells of patients with Alzheimer's disease, compared with control patients without Alzheimer's. Because of these findings, the authors of this study concluded, ***"these data suggest that glutathione depletion may contribute to the pathogenesis of Alzheimer's in males."***

OPTIMIZING GLUTATHIONE TO PROTECT AGAINST MILD COGNITIVE IMPAIRMENT

It should be clear in the face of this mounting scientific evidence that maintaining optimal levels of glutathione is vital to your brain health. There are multiple ways to effectively increase your glutathione levels through natural supplements. One way to maintain high glutathione levels is through the use of two powerful antioxidants, lipoic acid and acetyl-L-carnitine.

Multiple studies have shown that acetyl-L-carnitine and lipoic acid may offer health benefits through their ability to increase glutathione levels.[14,16] In one study, researchers showed that lipoic acid given to aging rats successfully reversed age-related decline in glutathione levels in both the brain and heart, leading the authors of the study to conclude that ***"lipoic acid is an effective agent to restore both the age-associated decline in [antioxidant] ratio as well as increase cerebral [glutathione] levels that otherwise decline with age."***[14]

Lipoic acid and acetyl-L-carnitine also work on their own to combat free radicals. In a paper co-authored by the renowned researcher Dr. Bruce Ames, both lipoic acid and acetyl-L-carnitine were shown to significantly protect cells in rats against oxidative damage, leading the authors to conclude that " ..feeding old rats acetyl-L-carnitine plus lipoic acid lowers oxidants, neuron RNA oxidation, and mutagenic aldehydes…improves the age-associated decline in ambulatory activity and memory… and prevents…oxidative decay and dysfunction."[17] Finally, acetyl-L-carnitine may be useful in preventing mild cognitive impairment. A 6-12-month randomized, placebo-controlled trial using 1,500-3,000 mg/day of acetyl-L-carnitine showed that patients taking this safe and effective supplement had statistically greater scores on tests of memory and other cognitive functions.[18]

SAME—POSSIBLY THE MOST EFFECTIVE WAY OF BOOSTING BRAIN GLUTATHIONE

A study published in Germany evaluated the brains of rodents who received SAMe (S-adenosylmethionine) compared with a control group who did not get SAMe.[19] The results showed that:

1. SAMe increased glutathione levels by 50% and antioxidant glutathione enzyme activity by 98%.
2. SAMe decreased a measurement of free-radical activity by 46%.
3. SAMe inhibited lipid peroxidation by 55% in culture.

This rodent study showed that SAMe inhibits lipid peroxidation and enhances the glutathione antioxidant system specifically in the brain.[19]

The multi-faceted benefits of SAMe in protecting the brain, the liver, and the joints while improving mood have motivated many health-conscious people to take it daily.

PROTECTING BRAIN CELL MEMBRANES

Ever hear your mainstream physician talk about phosphatidylserine? Probably not, since like other supplements, it is not a patentable substance, and therefore has been dismissed by drug companies. Yet phosphatidylserine has been shown in multiple studies to be another safe and effective nutrient in warding off the cognitive decline seen in aging, including mild cognitive impairment. Phosphatidylserine—a phospholipid that is actually a major component of brain neuronal membranes—has been shown in animal studies to reduce many of the effects of aging on the brain.[20] Fortunately, these effects seem to similarly apply to humans. In double-blind, placebo-controlled studies conducted in Italy, patients (aged 55-80 years old) with mild cognitive impairment who took 300 mg/day of phosphatidylserine consistently scored higher in memory retention tests than those taking placebo.[21-23]

MILD COGNITIVE IMPAIRMENT—A REAL DISEASE WITH POTENTIALLY DEADLY CONSEQUENCES

Those in mainstream medicine typically insist on large, double-blind, placebo-controlled, randomized, multicenter studies before determining whether or not a treatment—or supplement—is worthwhile. While I have nothing against these types of studies—and agree with my mainstream colleagues that they are quite useful—I feel it is foolish at best and deadly at worst to wait until these studies are completed in order to recommend certain supplements for conditions in which mainstream medicine has no answers—such as mild cognitive impairment. A number of readily available supplements have been found in multiple studies to be potentially useful in preventing mild cognitive impairment and Alzheimer's disease. Until those in mainstream medicine can offer a safe, effective, and inexpensive alternative, I feel that it is my duty as a physician to inform my patients of this vital information to help prevent the loss of their memory and therefore, the loss of themselves.

If you have any questions on the scientific content of this article, please call a Life Extension Health Advisor at 1-800-226-2370.

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