

LE Magazine December 2006

## REPORT

### The Deadly Connection Between Diabetes and Alzheimer's

By Edward R. Rosick, DO, MPH, DABHM



With skyrocketing incidence rates that are expected to soar even higher in the future, diabetes is rapidly transforming the health landscape of the United States and other Western nations. It is no exaggeration to say that diabetes now looms as one of the most costly, destructive medical epidemics of the early twenty-first century.

Those affected with diabetes face a host of insidious health threats that include heart disease, impotence, stroke, and blindness, to name just a few. Even worse, new research suggests that those with insulin resistance or diabetes are at significantly higher risk of developing one of today's most devastating and incurable neurological disorders: Alzheimer's disease.

The emerging connection between diabetes and Alzheimer's is yet another compelling reason for those who value their health to address issues of impaired insulin sensitivity before it is too late. Although diabetes is an emerging epidemic, it is also wholly preventable and reversible through strategies that incorporate dietary changes, lifestyle modifications, and nutritional supplementation.

Achieving and maintaining optimal blood sugar and insulin sensitivity may thus be one of the most important steps you can take to protect yourself against an array of life-threatening conditions—including diabetes and mind-destroying dementia.

#### TYPE II DIABETES FUELS A GROWING EPIDEMIC

It is frightening, but unsurprising, to think that almost everyone in America knows someone—a friend, relative, coworker—who has diabetes. Nearly 21 million adults and children in the United States have diabetes, while an estimated 41 million people between the ages of 40 and 74 have pre-diabetes.<sup>1</sup>

Type I diabetes, which affects fewer than 2 million people in the US, occurs when the body does not produce adequate levels of insulin, a hormone secreted by the pancreas. If not present, insulin cannot do its job of moving glucose (blood sugar) into cells. Since all cells in the body use glucose as fuel, not producing enough insulin can be a deadly problem.

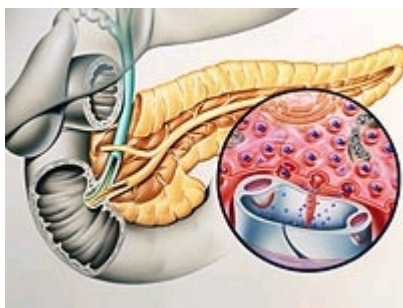
The far more common form of the disease is type II diabetes. In the later stages of type II diabetes, people will often need insulin; in the early stages, however, the pancreas often secretes too much insulin. This occurs because of insulin resistance, a condition in which the body cannot utilize insulin efficiently to move glucose into cells, causing the pancreas to work harder at its job. Over a period of years and decades, the pancreas is no longer able to produce sufficient insulin. It is at this point that type II diabetics require insulin injections, just as type I diabetics require insulin.



It should be noted that while nearly all people with type II diabetes are insulin resistant, not all people with insulin resistance—approximately 50 million Americans—have type II diabetes. Given national trends toward ever more obesity and sedentary lifestyles, however, many of these individuals are well on their way to developing full-blown type II diabetes.

#### DIABETES PROMOTES DAMAGING ADVANCED GLYCATION END PRODUCTS

The many ways in which insulin resistance and diabetes can damage one's health are now widely recognized by most doctors. High blood sugar can damage your blood vessels and nerves, which in turn can lead to such debilitating conditions as blindness, kidney damage, and heart disease, and eventually to an early death.<sup>1</sup> However, what many mainstream physicians may not be aware of is that diabetes can also lead to the formation of damaging substances known as advanced glycation end products, or AGEs.



The pancreas (yellow) is situated in the loop of the duodenum (grey tube) and below the liver and gall bladder. The pancreas produces digestive enzymes that pass into the intestine through the pancreatic duct (yellow tube). Production of the hormone insulin by the endocrine pancreas is shown inset. A beta cell (red) secretes insulin (blue) into a capillary (grey). Insulin regulates the levels of sugar (glucose) in the bloodstream. Image by John Bavosi /SPL.

Advanced glycation end products are sugar-derived substances that form in the human body through the interaction between carbohydrates and proteins, lipids, or nucleic acids such as DNA. Once formed, AGEs adversely affect the structure and function of proteins and the tissues that contain these proteins. Considering that proteins are present everywhere in the human body, the importance and destructive potential of advanced glycation end products cannot be underestimated. Recent studies have shown that both the formation and accumulation of AGEs are enhanced in diabetes.<sup>2</sup> These proteins damaged by the glycation process may thus play an important role in the pathogenesis of diabetic complications—and, as we shall see, in the development of Alzheimer's disease.

Advanced glycation end products become even more destructive when coupled with free radicals formed during cellular energy production. These highly reactive agents produce oxidative stress that can cause cellular damage. Researchers now believe that oxidative stress may be involved in the formation of advanced glycation end products, which in turn may induce even more oxidative stress. In fact, most AGEs that accumulate in proteins are produced under conditions of high oxidative stress. New evidence shows that oxidative stress may be an important causative factor in both insulin resistance and type II diabetes.<sup>3,4</sup>

### **OXIDATIVE STRESS, AGES IMPLICATED IN DEVELOPMENT OF ALZHEIMER'S**

Alzheimer's disease is a devastating neurological condition that slowly but inexorably destroys the ability to think, eventually robbing a person of both his memory and ability to function independently. Alzheimer's delivers a crushing blow not only to the affected individual, but also to family members, who frequently struggle to provide the ever-growing levels of care required by the patient.

First described by Dr. Alois Alzheimer a century ago, Alzheimer's disease now affects more than 15 million people worldwide. With the rapid aging of society (an estimated 30% of the US population will be 65 or older by 2050), upwards of 14 million Americans are projected to develop Alzheimer's in the coming decades.<sup>5-7</sup>

While medical researchers have yet to pinpoint a single cause of Alzheimer's disease, they have uncovered some of the basic biochemical processes that underlie the hallmark mental changes seen in Alzheimer's.

First, Alzheimer's sufferers exhibit a marked decline in levels of acetylcholine, a neurotransmitter (that is, a chemical messenger of the nervous system) that is vitally important to memory formation and retention in certain regions of the brain.<sup>8</sup> Second, Alzheimer's patients demonstrate an accumulation of harmful beta amyloid deposits, or senile plaques, in the brain.<sup>9</sup> Third, brain autopsies of Alzheimer's patients show signs of significant oxidative damage induced by free radicals. Finally, new research indicates that advanced glycation end products may also initiate this dreaded condition.<sup>10</sup>

A newly published review article examines the role of AGEs and oxidative stress in Alzheimer's disease.<sup>10</sup> Scientists found that advanced glycation end products were present in higher amounts in the biopsied brains of patients who had died from Alzheimer's than in those who died from other causes. They also presented evidence that AGEs form in the brains of Alzheimer's sufferers early in the disease process.

## **DIABETES AND ALZHEIMER'S: WHAT YOU NEED TO KNOW**

- Insulin resistance and diabetes have reached epidemic proportions in the United States, with nearly one third of the population already affected, a proportion expected to grow much larger in the future. Diabetes is associated with adverse conditions such as stroke, heart disease, and blindness.
- As the baby-boom generation continues to age, the prevalence of Alzheimer's disease is expected to skyrocket. Alzheimer's is an incurable disease that leads to a loss of memory, cognition, and the ability to function independently.
- Diabetes and Alzheimer's disease share several biochemical similarities, including oxidative stress and the presence of damaging molecules known as advanced glycation end products (AGEs).
- Scientists have discovered that type II diabetes is associated with an increased risk of developing Alzheimer's disease.
- Strategies to prevent or manage insulin resistance and diabetes may hold promise in protecting against Alzheimer's disease. These include avoiding saturated fat, increasing consumption of monounsaturated and omega-3 fatty acids, instituting a program of regular exercise, and utilizing natural therapeutics that have been demonstrated to promote healthy blood sugar, including magnesium, chromium, lipoic acid, cinnamon, and carnosine.



## NEW RESEARCH, EARLIER STUDIES SUPPORT DIABETES-ALZHEIMER'S LINK

While declining levels of acetylcholine and formation of beta amyloid plaques in the brain are characteristic of Alzheimer's, oxidative damage and the accumulation of advanced glycation end products occur in both Alzheimer's disease and diabetes. These biochemical similarities may be a telling link between the two seemingly different diseases.

At an Alzheimer's Association international conference held in Madrid in July 2006, scientists presented multiple studies linking diabetes and Alzheimer's disease.<sup>11</sup> For example, Swedish scientists unveiled findings associating borderline diabetes with an increased risk of developing dementia and Alzheimer's, particularly in those with very high systolic blood pressure. Over the course of their nine-year study, borderline diabetes was associated with a nearly 70% greater risk of developing dementia and Alzheimer's in individuals over the age of 75. The risk was even more pronounced in those with severely elevated systolic blood pressure (180 mmHg or above). The authors concluded, "Our findings have significant implications for public health because some studies show that impaired glucose regulation can be improved by lifestyle changes. Our findings also highlight the need to detect borderline diabetes in order to proactively address both type II diabetes and dementia."<sup>11</sup>

Scientists from Kaiser Permanente in Oakland, CA, reported that diabetic individuals with very poor blood sugar control experience a dramatically increased risk of dementia and Alzheimer's. Their eight-year study, which tracked 22,852 patients aged 50 or above with type II diabetes, sought to determine whether elevated glycosylated hemoglobin, a marker of long-term blood sugar control, correlated with an increased risk of dementia. They found that patients with very poor blood sugar control were more likely to develop dementia. Compared to those with normal glycosylated hemoglobin levels (< 7), those with levels greater than 12 were 22% more likely to develop dementia, while those with levels greater than 15 were 78% more likely to develop dementia. According to the study authors, "Effective blood sugar control may lower risk of another diabetes-associated complication—dementia."

Researchers from the Mount Sinai School of Medicine in New York City discussed the link between diabetes-related toxins and impaired memory function. Advanced glycation end products are increased in people with diabetes, as well as in those with cardiovascular and kidney disease. They are also found in the brains of people with Alzheimer's, and laboratory findings suggest that AGEs may contribute to the formation of Alzheimer's plaques and tangles. The researchers evaluated nearly 200 cognitively healthy people aged 70 or older using tests of memory and thinking ability, and measured AGE levels in their blood. They found that those with the highest AGE levels fared significantly worse on six different tests than those with low AGE levels. This relationship could not be explained by factors such as gender, educational level, heart disease, or related conditions such as high blood pressure. The researchers concluded that dietary and lifestyle interventions to decrease advanced glycation end products in the blood deserve further study for preventing or delaying Alzheimer's disease.<sup>11</sup>

Investigators from the Boston University School of Public Health reported that individuals who use thiazolidinedione (TZD) drugs to lower their blood sugar experienced lower rates of Alzheimer's disease. TZDs are used with diet and exercise to treat type II diabetes, either alone or in combination with other drugs. They lower blood sugar by helping the body's cells use insulin more efficiently to remove excess sugar from the blood. Scientists believe that TZDs may also influence inflammation and other brain cell processes that could be related to the development of Alzheimer's.

The Boston University researchers studied diabetes patients treated with TZDs to determine whether TZDs were associated with fewer new cases of Alzheimer's. Using data from the US Dept. of Veterans Affairs, they identified 142,328 patients who received a first prescription for TZDs or insulin without prior prescriptions for either medication or a recorded diagnosis of Alzheimer's. The patients were then followed and monitored for an Alzheimer's diagnosis. The researchers found that patients who were prescribed TZDs had lower rates of Alzheimer's. They estimated that there were nearly 20% fewer new cases of Alzheimer's in veterans taking TZDs than in those taking insulin. Similar results were found in a separate comparison between TZD users and patients starting metformin, another drug used to treat diabetes. According to the researchers, "These results are encouraging and suggest that TZDs may provide important benefits beyond their use in treating diabetes."<sup>11</sup>



While recent findings linking diabetes and Alzheimer's disease may seem like a revelation, previous research findings suggest a connection between the two seemingly disparate conditions.

One widely referenced work from 1999 that uncovered an association between diabetes and neurodegenerative disease is the Rotterdam Study. In this landmark trial conducted in the Netherlands, 6,370 elderly men and women were tracked over an average of two years. During this period, researchers noted subjects who became demented from Alzheimer's or had diabetes. They concluded that having diabetes almost doubled the subjects' risk of dementia.<sup>12</sup>

A study in 2004 examined the association between type II diabetes, high insulin levels, and Alzheimer's risk. A total of 683 men and women were followed and examined for signs of Alzheimer's and increased insulin levels. As in the earlier study, the scientists found that high insulin levels, which are intimately connected to type II diabetes, were significantly correlated with a higher risk of developing Alzheimer's.<sup>13</sup>

The possible mechanism by which high insulin levels are linked to Alzheimer's was elucidated in a 2005 study published in the Archives of Neurology. Researchers showed that by mimicking high insulin levels (such as those seen in patients with insulin resistance and type II diabetes) in 16 healthy men ranging in age from 55 to 81, they were able to elevate inflammatory markers and beta amyloid levels in the brain, two characteristics of Alzheimer's disease.<sup>14</sup>

## **AN IMMINENT EXPLOSION IN ALZHEIMER'S CASES?**

The connection between diabetes and Alzheimer's has major public health implications, as the baby-boomer generation approaches 60, the age of highest Alzheimer's disease risk. Since nearly one third of Americans have higher-than-normal blood sugar or diabetes, a confirmed link between diabetes and Alzheimer's could foretell a dramatic increase in Alzheimer's cases.<sup>11</sup>

Researchers have thus proposed that existing interventions to prevent and treat diabetes may prove useful in averting Alzheimer's disease. Since many such therapies—including dietary changes, exercise, nutrients, and drugs—already have years of research and clinical application behind them, this could allow for rapid testing of their efficacy against Alzheimer's.<sup>11</sup>

# REPORT

## The Deadly Connection Between Diabetes and Alzheimer's

By Edward R. Rosick, DO, MPH, DABHM

### EFFECTS OF DIET IN MAINTAINING HEALTHY BLOOD SUGAR

Now that diabetes appears to be associated with Alzheimer's, it is imperative to take action to protect against this burgeoning epidemic. The first two steps are ones that almost everyone can implement: eat a healthy diet and exercise regularly.

The typical modern American diet, with its preponderance of meats, trans-fatty acids, and sugar, significantly increases the prevalence of insulin resistance and type II diabetes.<sup>15</sup> Additionally, the American diet is typically low in healthful monounsaturated and omega-3 polyunsaturated fats, which are critical to optimal health and can also help improve insulin resistance.

Trans fats, found in hydrogenated vegetable oils and hard-stick margarine, worsen insulin sensitivity. By contrast, monounsaturated fats, such as those in olive oil, almonds, and avocados, improve insulin sensitivity.<sup>16</sup> Similarly, studies suggest that minimizing saturated fats, found in high amounts in animal products such as red meat and whole milk, may help to lessen one's risk for type II diabetes.<sup>16</sup>

Omega-3 fatty acids from fish oil, such as EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid), may be helpful in maintaining healthy glucose levels and optimal insulin action. Studies suggest that intake of omega-3 fats from fish oil is associated with accelerated glucose uptake and maintenance of normal glucose metabolism. Additionally, fish oil enhances insulin secretion from the cells of the pancreas.<sup>17</sup>

A healthy diet may thus help guard against diabetes and, by association, Alzheimer's disease.

### REGULAR EXERCISE IMPROVES INSULIN RESISTANCE

In addition to eating a diet that is low in saturated fat and sugar, high in monounsaturated fats, and rich in vegetables, fruits, and fiber, getting regular exercise is another vitally important way to both prevent and correct insulin resistance.

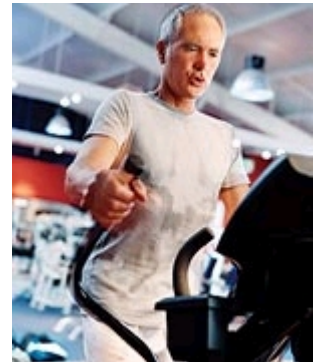
Exercise can improve insulin sensitivity in skeletal muscle and fat tissue, and has been shown to consistently reduce insulin and fasting blood sugar levels.<sup>18</sup> Moreover, recent studies demonstrate that a healthy diet and regular exercise can improve cognition in people who are at high risk for insulin resistance and diabetes.<sup>19</sup> In one such study, researchers showed that a group of adults with insulin resistance who followed a basic American Heart Association diet and exercised three times a week on a treadmill for one hour had increased memory retention compared to adults in a control group. The authors concluded that exercise and good nutrition may facilitate improvements in memory for older adults who are at high risk for type II diabetes. These findings may also have implications for guarding against the development of impaired memory and Alzheimer's.

### MAGNESIUM, CHROMIUM FIGHT INSULIN RESISTANCE AND DIABETES

Magnesium and chromium are two important minerals that have significant effects on insulin resistance and type II diabetes.

Multiple studies attest to the importance of magnesium supplementation, as exemplified by a controlled, randomized, double-blind trial published in 2003 in the journal *Diabetes Care*.<sup>20</sup> In this study, 63 people with type II diabetes were randomly assigned to receive either 2.5 grams of magnesium or a placebo daily for 16 weeks. At the end of the study period, scientists found that those who took the magnesium supplements had statistically significant improvements in insulin sensitivity, indicating better metabolic control of their diabetes.

Chromium has also been shown to be safe and effective in the management of patients with insulin resistance and type II diabetes. In a study of 180 men and women with type II diabetes, those who took 200-1000 mcg of chromium daily showed numerous improvements in blood sugar metabolism. These beneficial changes included significant decreases in levels of fasting glucose, fasting insulin, and two-hour insulin.<sup>21</sup>



By improving insulin sensitivity, magnesium and chromium may help prevent conditions associated with insulin resistance,

including inflammation, diabetes, and Alzheimer's.

## LIPOIC ACID PROVIDES POWERFUL ANTIOXIDANT PROTECTION

Lipoic acid, a powerful antioxidant, is also known for its ability to improve insulin sensitivity. In one study, 74 patients with type II diabetes were randomly assigned to receive either a placebo or 600, 1200, or 1800 mg a day of alpha-lipoic acid.<sup>22</sup> After four weeks, those receiving alpha-lipoic acid supplements had statistically improved insulin sensitivity. All three doses of alpha-lipoic acid were effective in improving insulin sensitivity.

Studies show that alpha-lipoic acid also helps protect help the brain against damage caused by free-radical-induced oxidative stress, which could have important implications for its potential role in protecting against Alzheimer's disease.<sup>23,24</sup>

By restoring insulin sensitivity and protecting the brain against oxidative stress, alpha-lipoic acid shows promise as a weapon against both diabetes and Alzheimer's.

## CINNAMON PROMOTES HEALTHY BLOOD SUGAR METABOLISM

Cinnamon, a common spice used the world over, has shown value in managing insulin resistance and type II diabetes in both laboratory and human studies. Cinnamon contains many beneficial chemical constituents such as flavonoids that act as potent antioxidants.



Cinnamon

A recent randomized, placebo-controlled study published in *Diabetes Care* examined the effects of supplementing with 1, 3, or 6 grams of cinnamon daily in 60 middle-aged men and women with type II diabetes.<sup>25</sup> At the end of the 40-day study, the subjects who took cinnamon at all three dosages significantly decreased their fasting serum glucose, triglycerides, total cholesterol, and low-density lipoprotein (LDL).

Cinnamon's ability to promote healthy blood sugar metabolism suggests a therapeutic role for this spice in preventing and managing insulin resistance and diabetes. Its efficacy in supporting optimal blood sugar levels further suggests a potential role in averting the dangers of Alzheimer's disease.

## CARNOSINE COUNTERS DAMAGING EFFECTS OF GLYCATION

Growing evidence demonstrating the damaging effects of advanced glycation end products—and the strong association between AGEs, free radicals, and crippling diseases such as diabetes and Alzheimer's—underscore the need to protect against these destructive chemicals. One way to do this is by supplementing with carnosine.

Carnosine, a natural compound made up of the amino acids beta-alanine and L-histidine, is present in high concentrations in brain and skeletal muscle tissue. Scientists have shown that carnosine can inhibit free-radical-induced cellular damage,<sup>26</sup> delay the impairment of eyesight associated with aging,<sup>27</sup> and even extend the life span of mammals.<sup>28</sup> Carnosine confers these beneficial effects through its ability to prevent the formation of advanced glycation end products.

## CURCUMIN PROMOTES HEALTHY BLOOD SUGAR, PROTECTS NERVOUS SYSTEM

Derived from the curry spice turmeric, curcumin is a potent antioxidant whose ability to relieve inflammation and help fight cancer has been the subject of much scientific study.<sup>32</sup> New evidence suggests curcumin may also be an important ally in averting diabetes and Alzheimer's disease.

Scientists have noted that curcumin has numerous beneficial effects on blood sugar metabolism. Using animals with experimentally induced diabetes, they found that curcumin normalized blood sugar levels and restored enzymes involved in blood sugar metabolism to normal levels of activity.<sup>33</sup> Other researchers have found that curcumin helps relieve oxidative stress related to elevated glucose levels, thus preventing some of the biochemical dysfunction associated with diabetes.<sup>34</sup>

In addition to supporting healthy blood sugar levels, curcumin may help to protect the nervous system and avert Alzheimer's disease. Scientists report that curcumin's antioxidant and anti-inflammatory effects offer important, targeted support for the health of the brain and nervous system. Additionally, laboratory and animal studies indicate that curcumin helps prevent the dangerous effects of one of the hallmark pathological changes of Alzheimer's disease: beta amyloid deposits in the brain.<sup>35</sup>

By supporting healthy blood sugar metabolism and fighting the effects of inflammation and beta amyloid in the brain, curcumin offers promise in the fight against both diabetes and Alzheimer's disease.

Experimental studies have shown that carnosine specifically protects the brain against damage induced by free radicals and AGEs, a finding that may have important implications for the prevention and treatment of Alzheimer's disease.<sup>29-31</sup> One study showed that carnosine protects the brain against the toxic effects of malondialdehyde, an AGE-like compound that is formed when lipids react with free radicals.<sup>30</sup> Using cultured rat brain cells, researchers demonstrated that carnosine protects brain cells from malondialdehyde-induced toxicity and prevents this compound from dangerously altering proteins in the body.



A recent article examined carnosine's protective effects against beta amyloid.<sup>31</sup> Using rat brain cells in the laboratory, researchers showed that introducing beta amyloid to the cultures produced measurable toxic effects. The researchers then demonstrated that damage to the brain cells could be substantially mitigated by adding carnosine to the mixture, leading them to conclude that carnosine protects brain cells by quenching oxidative stress and preventing damaging glycation reactions—both of which are implicated in the neuronal cell damage characteristic of Alzheimer's disease. Carnosine therefore appears to be a useful therapeutic in protecting neurons against the toxic effects of beta amyloid.

By inhibiting oxidative stress and AGE formation, carnosine may be a powerful weapon against both diabetes and Alzheimer's disease.

## LIMITING FORMATION OF AGES PROTECTS AGAINST DIABETES, ALZHEIMER'S, AND AGE-RELATED DISEASE

One critically important factor linking aging, diabetes, and Alzheimer's disease is the formation, accumulation, and receptor binding of advanced glycation end products (AGEs).<sup>36</sup> Formed through the interaction of sugars with proteins, lipids, or nucleic acids, AGEs alter the structure and function of proteins, rendering them less capable of carrying out their many crucial functions throughout the body.

The formation of advanced glycation end products throughout the body contributes to the aging of biological macromolecules and tissues. Two extracellular proteins, collagen and elastin, are particularly affected. AGE-related changes to these proteins are believed to contribute to stiffness of blood vessels and the urinary bladder, as well as impaired functioning of the kidneys, heart, retina, and other organs and tissues. Furthermore, damaging glycation reactions trigger inflammatory signaling, which scientists believe could provoke tissue damage and cancers.<sup>37</sup>



In diabetes, the rapid formation and accumulation of AGEs contribute to complications of the disease, including injury to small blood vessels (microangiopathy) that impairs kidney and eye health. Advanced glycation end products have similarly devastating effects on the nervous system, where they may contribute to degenerative processes. A particularly dangerous form of AGE that has toxic effects against neurons has been found to accumulate in the region of the brain associated with memory and emotion, an area that sustains damage in Alzheimer's disease.<sup>36</sup> Furthermore, AGEs promote the accumulation and cross-linking of harmful beta amyloid plaques in the brain, which may contribute to the pathological changes and progressive dementia of Alzheimer's disease.<sup>38</sup> Scientists report that AGEs may also play a role in amyotrophic lateral sclerosis, also known as Lou Gehrig's disease.<sup>36</sup>

Given the crucial role that advanced glycation end products play in aging, diabetes, and Alzheimer's disease, strategies to prevent their formation are more important than ever. Scientists have identified numerous dietary and nutritional approaches that may help protect against AGEs.

Since high blood sugar contributes to the formation of advanced glycation end products, strategies to maintain optimal blood sugar levels are crucial. In addition to those formed within the body, AGEs can also be introduced by external sources. For example, tobacco smoke contains precursors to advanced glycation end products, which increase AGE levels in the body. Foods that have been subjected to processing and heat also act as sources of advanced glycation end products.<sup>39</sup> Additionally, foods high in protein and fat are rich dietary sources of AGEs.<sup>40</sup> A dietary strategy for minimizing exposure to AGEs should emphasize fresh foods that have been cooked with brief applications of heat.<sup>39</sup>

One of the best-known nutrients for protecting against the damaging effects of AGEs is carnosine.<sup>26-31</sup> Other strategies for fighting advanced glycation end products include antioxidants, B vitamins, and alagebrium, a novel remedy currently under investigation. Specifically, the antioxidants vitamin C and vitamin E have been reported to inhibit the formation of AGEs.<sup>41</sup> Scientists report that the B vitamins pyridoxamine (a form of vitamin B6) and benfotiamine (a fat-soluble form of vitamin B1) show promise in reducing the accumulation of AGEs.<sup>42</sup> Alagebrium is currently undergoing clinical trials, with evidence suggesting that it is capable of breaking AGE crosslinks.<sup>42</sup>

Given the devastating effects of advanced glycation end products in promoting aging and disease processes, protecting yourself against them should be considered a core element of every anti-aging strategy.

## CONCLUSION

Growing scientific evidence suggests that diabetes and Alzheimer's disease—two epidemic yet seemingly different disorders that threaten the health of tens of millions of Americans—may not be so dissimilar after all. These two apparently divergent conditions share a striking number of biochemical similarities, and scientists increasingly believe that the two diseases may be closely related.

Given the growing prevalence of insulin resistance and diabetes in the United States and other Western nations, this news has far-reaching implications. Fortunately, substantial research demonstrates that a program incorporating dietary modifications, regular exercise, and scientifically substantiated nutritional supplements can help aging adults to greatly lessen their risk for the twin afflictions of diabetes and Alzheimer's disease.

*Edward R. Rosick, DO, MPH, DABHM, is a board-certified physician in preventive and holistic medicine, and assistant professor of medicine at Michigan State University.*

---

## References

---

1. Available at: <http://diabetes.niddk.nih.gov/dm/pubs/statistics/index.htm>. Accessed September 29, 2006.
2. Ramasamy R, Vannucci SJ, Yan SS, et al. Advanced glycation end products and RAGE: a common thread in aging, diabetes, neurodegeneration, and inflammation. *Glycobiology*. 2005 Jul;15(7):16R-28R.
3. Opara EC. Oxidative stress, micronutrients, diabetes mellitus and its complications. *J R Soc Health*. 2002 Mar;122(1):28-34.
4. Houstis N, Rosen ED, Lander ES. Reactive oxygen species have a causal role in multiple forms of insulin resistance. *Nature*. 2006 Apr 13;440(7086):944-8.
5. Available at: <http://www.alz.org/AboutAD/statistics.asp>. Accessed September 29, 2006.
6. Grundman M, Thal LJ. Treatment of Alzheimer's disease: rationale and strategies. *Neurol Clin*. 2000 Nov;18(4):807-28.
7. Mayeux R, Sano M. Treatment of Alzheimer's disease. *N Engl J Med*. 1999 Nov 25;341(22):1670-9.
8. Wenk GL. Neuropathological changes in Alzheimer's disease: potential targets for treatment. *J Clin Psychiatry*. 2006;67 Suppl 3:3-7;quiz 23.
9. Masters CL, Cappai R, Barnham KJ, Vilmagne VL. Molecular mechanisms for Alzheimer's disease: implications for neuroimaging and therapeutics. *J Neurochem*. 2006 Jun;97(6):1700-25.
10. Moreira PI, Smith MA, Zhu X, et al. Oxidative stress and neurodegeneration. *Ann NY Acad Sci*. 2005 Jun;1043:545-52.
11. Available at: [http://www.alz.org/icad/newsreleases/071606\\_noon\\_diabetesandad.asp](http://www.alz.org/icad/newsreleases/071606_noon_diabetesandad.asp). Accessed September 29, 2006.
12. Ott A, Stolk RP, van HF, et al. Diabetes mellitus and the risk of dementia: The Rotterdam Study. *Neurology*. 1999 Dec 10;53(9):1937-42.
13. Luchsinger JA, Tang MX, Shea S, Mayeux R. Hyperinsulinemia and risk of Alzheimer disease. *Neurology*. 2004 Oct 12;63(7):1187-92.
14. Fishel MA, Watson GS, Montine TJ, et al. Hyperinsulinemia provokes synchronous increases in central inflammation and beta-amyloid in normal adults. *Arch Neurol*. 2005 Oct;62(10):1539-44.
15. Available at: [http://www.webmd.com/content/article/5/1680\\_51079.htm](http://www.webmd.com/content/article/5/1680_51079.htm). Accessed September 29, 2006.

16. Rivellese AA, Lilli S. Quality of dietary fatty acids, insulin sensitivity and type 2 diabetes. *Biomed Pharmacother*. 2003 Mar;57(2):84-7.
17. [No authors listed]. Monograph. Fish oil. *Altern Med Rev*. 2000 Dec;5(6):576-80.
18. Kelly GS. Insulin resistance: lifestyle and nutritional interventions. *Altern Med Rev*. 2000 Apr;5(2):109-32.
19. Watson GS, Reger MA, Baker LD, et al. Effects of exercise and nutrition on memory in Japanese Americans with impaired glucose tolerance. *Diabetes Care*. 2006 Jan;29(1):135-6.
20. Rodriguez-Moran M, Guerrero-Romero F. Oral magnesium supplementation improves insulin sensitivity and metabolic control in type 2 diabetic subjects: a randomized double-blind controlled trial. *Diabetes Care*. 2003 Apr;26(4):1147-52.
21. Anderson RA, Cheng N, Bryden NA, et al. Elevated intakes of supplemental chromium improve glucose and insulin variables in individuals with type 2 diabetes. *Diabetes*. 1997 Nov;46(11):1786-91.
22. Jacob S, Ruus P, Hermann R, et al. Oral administration of RAC-alpha-lipoic acid modulates insulin sensitivity in patients with type-2 diabetes mellitus: a placebo-controlled pilot trial. *Free Radic Biol Med*. 1999 Aug;27(3-4):309-14.
23. Arivazhagan P, Panneerselvam C. Alpha-lipoic acid increases Na+K+ATPase activity and reduces lipofuscin accumulation in discrete brain regions of aged rats. *Ann N Y Acad Sci*. 2004 Jun;1019:350-4.
24. Lovell MA, Xie C, Xiong S, Markesbery WR. Protection against amyloid beta peptide and iron/hydrogen peroxide toxicity by alpha lipoic acid. *J Alzheimers Dis*. 2003 Jun;5(3):229-39.
25. Khan A, Safdar M, li Khan MM, Khattak KN, Anderson RA. Cinnamon improves glucose and lipids of people with type 2 diabetes. *Diabetes Care*. 2003 Dec;26(12):3215-8.
26. Boldyrev AA, Stvolinsky SL, Tyulina OV, et al. Biochemical and physiological evidence that carnosine is an endogenous neuroprotector against free radicals. *Cell Mol Neurobiol*. 1997 Apr;17(2):259-271.
27. Wang AM, Ma C, Xie ZH, Shen F. Use of carnosine as a natural anti-senescence drug for human beings. *Biochemistry (Mosc.)*. 2000 Jul;65(7):869-71.
28. Stvolinskii SL, Fedorova TN, Yuneva MO, Boldyrev AA. Protective effect of carnosine on Cu,Zn-superoxide dismutase during impaired oxidative metabolism in the brain in vivo. *Bull Exp Biol Med*. 2003 Feb;135(2):130-2.
29. Dukic-Stefanovic S, Schinzel R, Riederer P, Munch G. AGES in brain ageing: AGE-inhibitors as neuroprotective and anti-dementia drugs? *Biogerontology*. 2001;2(1):19-34.
30. Hipkiss AR, Preston JE, Himswoth DT, Worthington VC, Abbot NJ. Protective effects of carnosine against malondialdehyde-induced toxicity towards cultured rat brain endothelial cells. *Neurosci Lett*. 1997 Dec 5;238(3):135-8.
31. Preston JE, Hipkiss AR, Himswoth DT, Romero IA, Abbott JN. Toxic effects of beta-amyloid(25-35) on immortalised rat brain endothelial cell: protection by carnosine, homocarnosine and beta-alanine. *Neurosci Lett*. 1998 Feb 13;242(2):105-8.
32. Singh S, Khar A. Biological effects of curcumin and its role in cancer chemoprevention and therapy. *Anticancer Agents Med Chem*. 2006 May;6(3):259-70.
33. Pari L, Murugan P. Effect of tetrahydrocurcumin on blood glucose, plasma insulin and hepatic key enzymes in streptozotocin induced diabetic rats. *J Basic Clin Physiol Pharmacol*. 2005;16(4):257-74.
34. Jain SK, Rains J, Jones K. Effect of curcumin on protein glycosylation, lipid peroxidation, and oxygen radical generation in human red blood cells exposed to high glucose levels. *Free Radic Biol Med*. 2006 Jul 1;41(1):92-6.
35. Ringman JM, Frautschy SA, Cole GM, Masterman DL, Cummings JL. A potential role of the curry spice curcumin in Alzheimer's disease. *Curr Alzheimer Res*. 2005 Apr;2(2):131-6.
36. Takeuchi M, Kikuchi S, Sasaki N, et al. Involvement of advanced glycation end-products (AGEs) in Alzheimer's disease. *Curr Alzheimer Res*. 2004 Feb;1(1):39-46.

37. Furber JD. Extracellular glycation crosslinks: prospects for removal. *Rejuvenation Res.* 2006 Summer;9(2):274-8.
38. Munch G, Kuhla B, Luth HJ, Arendt T, Robinson SR. Anti-AGEing defenses against Alzheimer's disease. *Biochem Soc Trans.* 2003 Dec;31(Pt 6):1397-9.
39. Peppas M, Uribarri J, Vlassara H. Glucose, advanced glycation end products, and diabetes complications: what is new and what works. *Clinical Diabetes.* 2003;21:186-7.
40. McCarty MF. The low-AGE content of low-fat vegan diets could benefit diabetics - though concurrent taurine supplementation may be needed to minimize endogenous AGE production. *Med Hypotheses.* 2005;64(2):394-8.
41. Qian P, Cheng S, Guo J, Niu Y. Effects of vitamin E and vitamin C on nonenzymatic glycation and peroxidation in experimental diabetic rats. *Wei Sheng Yan Jiu.* 2000 Jul;29(4):226-8.
42. Thomas MC, Baynes JW, Thorpe SR, Cooper MF. The role of AGEs and AGE inhibitors in diabetic cardiovascular disease. *Curr Drug Targets.* 2005 Jun;6(4):453-74.
43. Rivera EJ, Goldin A, Fulmer N, Tavares R, Wands JR, de la Monte SM. Insulin and insulin-like growth factor expression and function deteriorate with progression of Alzheimer's disease: link to brain reductions in acetylcholine. *J Alzheimers Dis.* 2005 Dec;8(3):247-68.
44. de la Monte SM, Tong M, Lester-Coll N, Plater M Jr, Wands JR. Therapeutic rescue of neurodegeneration in experimental type 3 diabetes: Relevance to Alzheimer's disease. *J Alzheimers Dis.* 2006 Nov;10(1):89-109.

All Contents Copyright © 1995-2009 Life Extension Foundation All rights reserved.

**LifeExtension**<sup>®</sup>

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.