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Change

The Prevention of Alzheimer's Disease

UCLA Study Shows Promising Data for the Reversal of Memory Loss

It used to be that the most common question I would be asked in the way of prevention was "Doc, how do I prevent cancer?" More recently, however, the most common question I get is "Doc, how do I prevent Alzheimer's disease?" And no wonder, because most of us know someone or have a loved one who has Alzheimer's disease and have experienced firsthand how this disease ravages the mind. In 2013, there were 5 million Americans living with Alzheimer's, and in 2050 this number is projected to almost triple to 14 million.

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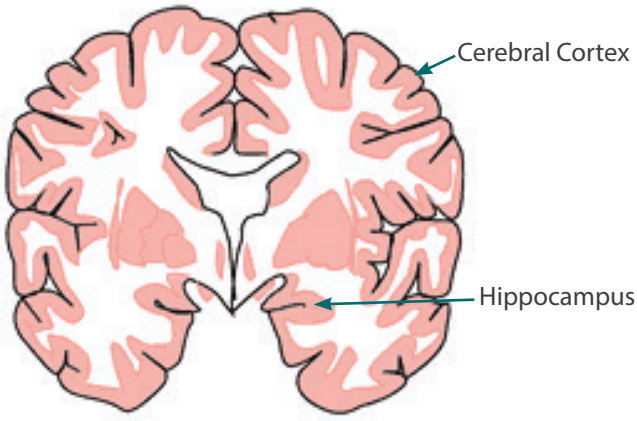
What is Alzheimer's Disease

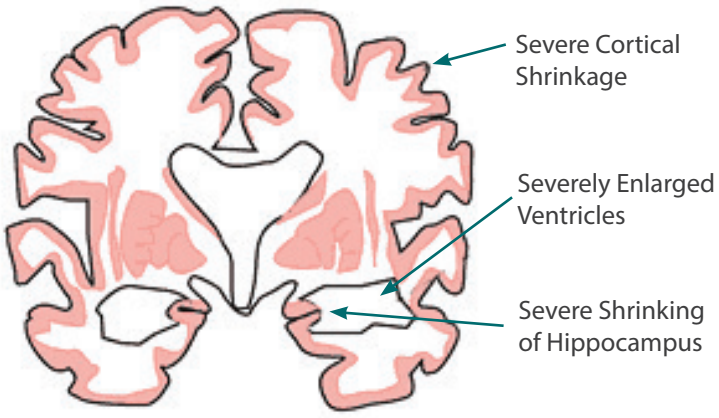
What is this dreaded disease and what can we do to prevent it? Alzheimer's disease is characterized by a sharp decline in the production of one of our main neurotransmitters, acetylcholine, and by the unchecked growth of two forms of protein deposits in the brain – beta-amyloid plaques and neurofibrillary tangles (tau protein tangles). No one knows for certain the exact cause of Alzheimer's disease, but there have been many hypotheses. Part of the difficulty in figuring out the cause of Alzheimer's is that it is very difficult to study the living brain. Most of the research done on Alzheimer's has been looking at the changes that have occurred in the brain after death. In fact, the disease was named after Alois Alzheimer, a German physician who discovered the formation of the abnormal proteins in the post-mortem brain of his patient Auguste Deter in 1906. Auguste had presented to the mental hospital five years earlier with delusional and paranoid behavior.

For a long time it was believed that the decrease in acetylcholine was the cause of the disease. Acetylcholine is the neurotransmitter that helps with movement, memory, attention, and creativity. This overlaps with what we see as some of the symptoms of Alzheimer's disease. The earliest symptoms are problems with decision making, attention, and flexibility of muscles. As the disease progresses, these changes become more severe and involve memory, mood, and difficulty moving in general – more symptoms of low acetylcholine. However, this theory of the cause of Alzheimer's has not maintained wide support because the medications aimed at raising levels of acetylcholine in the brain, such as Galantamine, have not been very effective.

Healthy Brain



Severe Alzheimer's Disease



In 2014, the estimated cost of Alzheimer's disease was $214 billion, and the cost of treating and caring for those with Alzheimer's disease is growing faster than any other illness. But even more challenging than the economic costs of Alzheimer's is the emotional toll it takes on family members and caregivers.

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Possible Causes of Alzheimer's

Another hypothesis of the cause of Alzheimer's is that the beta amyloid proteins cause dementia because they collect outside the nerve cells (neurons) in the brain and prevent the signals between neurons, blocking them from relaying messages. This communication breakdown could explain why Alzheimer's patients suffer progressive memory loss, confusion, and increasing difficulty completing daily tasks. However, beta-amyloid is a naturally occurring protein in the brain which is produced and then eliminated in the normal metabolic processes of the cells. It is believed that they even serve a protective function by acting as protein "guardians" to mute the body's auto-immune reactions. Beta-amyloid proteins also clean up inflammatory cytokines, or messengers, that are present after injury to the brain.

Finally, there are the neurofibrillary (tau) tangles. These proteins are also normally present in the brain. They provide the microtubule structure inside neurons that allow the nerve impulse to cross the synapse, or space, between neurons. In patients with Alzheimer's disease, the tau become hyperphosphorylated and begin to pair with other tau to form spaghetti-like strands which choke the neurons and disrupt the flow of electrical signals that travel through the nerve cell. With the formation of these neurofibrillary tangles, the skeletal structure of the neurons breaks down and the cells collapse and die. Tau tangles may be the true culprit behind memory loss, as they have been directly linked to cognitive deficits. Patients can have amyloid plaques and still function normally; however, once they have tau tangles, dementia is evident.

A New Theory Emerges

But a new theory is emerging that encompasses all of these theories. This theory has inflammation as the culprit behind all of these problems, so that Alzheimer's disease is really the brain on fire with inflammation. For two decades scientists have debated whether or not inflammation was the result of the formation of amyloid plaques and neurofibrillary tangles, or the cause of these protein developments. New research indicates that inflammation causes both. Studies done by Dr. Michael T. Heneka at the University of Bonn show that not only does inflammation fuel the fire once amyloid plaque formation has started, but inflammation can also cause the formation of beta-amyloid plaques. Let's take a closer look at this process.

The brain is an organ that was meant to be protected from infections and toxins by the blood-brain barrier. The blood-brain barrier is a layer of endothelial cells that form tight junctions between the blood stream and brain cells. In this manner, only small particles such as oxygen, carbon-dioxide, and hormones are allowed to cross into the brain, but not larger molecules such as bacteria and the antibodies needed to fight bacteria. One problem is that inflammation itself can weaken the blood brain barrier. When there is injury or infection in the body, inflammatory cytokines are produced in response. These are the messengers of the immune system, spreading the word throughout the body that there is an injury or an invasion. Many of these cytokines are cytotoxic to neurons – meaning they kill brain cells. Once they get past the now leaky blood-brain barrier, they start to cause damage to brain cells. A leaky blood-brain barrier also allows larger particles including bacteria and toxins to cross into the brain.

The brain responds by activating microglial cells. These are the immune cells of the brain and when they sense an injury or invader they work quickly to engulf invaders and swallow them up. As with any kind of immune response, the system works quite well except when there is chronic inflammation, or confounding genetic factors. With chronic inflammation, more amyloid is made by the neurons to help clean up the effects of the inflammation. The microglial cells are then supposed to clean up the amyloid and other molecular debris such as dead and dying nerve cells. However, with more amyloid formation the microglia have a harder time keeping up. Also, with chronic inflammation, the mi-

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croglia become hypervigilant and swing into action. They can become hyperstimulated, especially by two closely-related inflammation-promoting proteins, IL-2 and IL-3. Researchers have noticed that blocking these two proteins in Alzheimer's mice prevented the build-up of amyloid plaques with age. In mice whose brains already had a lot of plaque blocking these two proteins reduced some of the amyloid plaque and reversed some of the mice's cognitive defects.

Of course genetic defects can affect the likelihood of developing Alzheimer's. At least twenty-one genes have been linked to development of the disease. For example, 40 percent of people diagnosed with Alzheimer's disease have the APOE-4 gene. APOE is a lipoprotein that transports cholesterol and fat-soluble vitamins. Defects in the formation of this protein have been shown to increase the risk for atherosclerosis, cognitive defects, and Alzheimer's disease. Researchers at Harvard have discovered that families with the CD33 gene have a higher incidence of Alzheimer's disease, because when the CD33 gene is present, it further activates the microglia to change from being neuroprotective to being neurotoxic. Another gene, called ADAM10 makes an enzyme which prevents the formation of beta amyloid. When ADAM10 has a gene mutation, this enzyme actually works oppositely – it increases the formation of beta-amyloid.

UCLA Alzheimer's Study

If our health is truly a result of the interaction between our genes and the environment we put them in, then what can we do to prevent Alzheimer's disease? Clearly Alzheimer's disease will not be treated or prevented with a "single pill" approach. It also seems fairly clear that reducing inflammation in general reduces the risk of Alzheimer's. For the first time ever, a small study performed by Dr. Dale Bredesen of UCLA showed the reversal of memory loss associated with Alzheimer's disease. This study used a comprehensive approach which included diet, exercise, sleep optimization, vitamins, hormone replacement, along with stress management. Nine out of ten participants showed reversal in memory loss, and six were able to return to jobs that they had to discontinue due to cognitive decline. Obviously, more study is needed. However, to date over $1 billion has been spent in clinical trials for pharmaceuticals to reverse Alzheimer's and no drug has ever been found to stop, much less reverse, the progression of Alzheimer's disease.

The Bottom Line

So that's it! The bottom line is reducing inflammation and keeping the body functioning well. This is the crux of anti-aging medicine. This is why anti-aging medicine is so powerful – it is the way to prevent not only Alzheimer's, but every modern-day disease. Now when a patient asks me "Doc, what can I do to prevent Alzheimer's disease?" I tell them, "Everything that we do together to improve your health will help to prevent Alzheimer's disease!"

UCLA 36-Point Program

The program at UCLA involved a 36-point program. Every participant did not do every point. Each participant had a therapeutic program which was personalized for them so that compliance would be greater. I am happy to say that the list of points in this program reads like the textbook of anti-aging medicine. Here are some key points:

- Optimizing gut health by eliminated simple carbohydrates, gluten, and processed food from the diet to minimize inflammation and using probiotics
- Stress reduction – meditation, yoga, music, etc.
- Optimize sleep - eight hours per night, potentially using melatonin or tryptophan
- Exercise 30-60 minutes per day, 4-6 days per week
- Brain stimulation
- Homocysteine <7 using methyl B12, Methylfolate, Pyridoxyl 5 phosphate, TMG
- Serum B12 >500 using methyl B12
- CRP <1.0 using anti-inflammatory diet, curcumin, and omega-3 fatty acids
- Fasting insulin <7, HgbA1c <5.5 using diet as above
- Hormone balancing – optimizing thyroid, progesterone, pregnenolone, cortisol
- Optimizing Vitamin D3 levels 50-100ng/mL
- Optimize anti-oxidants using vitamin E, blueberries, N-acetyl cysteine, and vitamin C
- Optimizing mitochondrial function with Co Q10 or alpha lipoic acid, among others
- Exclude heavy metal toxicity by evaluating for lead, arsenic, cadmium, and mercury and chelating if needed