Bob's LAST MARATHON
Living the Alzheimer's Journey

TRANSCRIPT

# Lifestyle and Diet in Alzheimer's Disease Prevention

When we talk about memory and thinking as we get older, many people comment on "senior moments" or trouble juggling two things at once. What may surprise some people is that in fact most, but not all, of our cognitive abilities peak around age 20. A number of large and compelling studies show that memory span, processing speed, and attention all decline throughout our adulthood. But to keep it in perspective, this decline is within a narrow range—and some things do improve. Language, knowledge of the world, and judgment are examples of what does get better as we age.

But what happens when people fall off these normal curves? When there is a noteworthy change from a person's usual abilities, but they are still able to get things done, we call this mild cognitive impairment, or MCI. A person may take longer to get bills paid, do the shopping, or fix dinner, but they manage. If memory and thinking abilities decline to a point where they need help with these kinds of day-to-day activities, that's when we use the term *dementia*.

If you or someone you know is seeing a decline, it is important to get checked out by your health care provider. Some of these declines in mental abilities are caused by deficits that can be readily treated. An underactive thyroid gland or low vitamin B levels, for example, can affect neurological functioning and show themselves as MCI or dementia. These can be reversed. On the other hand, maybe 60 percent to 80 percent of cognitive decline in later life is due to Alzheimer's disease. About 20 percent to 40 percent may be due to vascular disease, mini-strokes, or small vessel disease, which used to be called hardening of the arteries. Five percent to 10 percent may be related to Parkinson's disease–related conditions, and another 5 percent or so to frontotemporal dementia. All in all, Alzheimer's disease, often mixed with vascular disease, is the major player.

The big question is, is there anything we can do to prevent disease or to slow disease progression? What can we do to lower risks for getting the disease?

There are a number of risk factors for developing dementia in later life. Some of these we can't control—like age, gender, and genetics. But there are other factors that we can change as individuals or as a society. One example is education; not just the years but the quality of education seems to be a risk factor for many subsequent health problems. Hearing loss in early, mid-, or late life increases our risk. Head injury, of course, damages the brain and makes it more vulnerable to the effects of any other diseases that come along. The cardiovascular risk factors associated with high blood pressure, diabetes, high cholesterol, obesity, low physical activity, and tobacco use all increase our risk for developing dementia and probably drive progression of dementia once we have it. We are also recognizing how depression, loneliness, and anxiety can increase our vulnerability to dementia, likely through stress mechanisms.

What is the evidence that modifying these risk factors can decrease the chances of our getting dementia? Several studies have attempted to associate intervention with results. One noted example is the FINGER study, conducted in about 1200 people in Finland who had either normal cognitive abilities or mild cognitive impairment and were at risk for dementia because of their age or some of the risk factors I just mentioned. People in the study were assigned to one of two groups—a regular health advice group or an intervention group where they had both personal and group sessions for diet planning and nutrition counseling, exercise training with physical therapists, and cognitive training and counseling sessions with different games and exercises. After two years, the people in the intervention group showed a small but significant performance

advantage in cognitive tests.

Another study, called PreDIVA, was conducted in the Netherlands in more than 3500 people, split into two groups, one that received usual care and the other a more intensive intervention program where they visited a trained nurse every four months for six years for lifestyle and medical care to address risk factors such as smoking, diet, exercise, weight, blood pressure, blood sugar, and lipids. This modest intervention ultimately did not show any difference between the groups in terms of how frequently people developed dementia.

A third study, conducted in almost 1700 people with memory complaints or mild cognitive impairment but not frank dementia, in different memory centers in France and Monaco, tested a combination of high-dose fish oil and group sessions involving physical activity and nutritional and lifestyle counseling, again with no statistically evident effect.

So, the jury is still out on whether making these types of modest changes in our health care and lifestyle in later life helps prevent or slow down dementia.

I am often asked about dietary supplements and natural products. There are literally hundreds of these on health food store and pharmacy shelves and online that are touted for their benefits for memory health and focus. In fact, in laboratory mice and Petri dishes, many of these have been shown to decrease the amyloid or tau pathology of Alzheimer's disease, reduce inflammation in the brain, improve metabolism, improve blood flow to the brain, or promote synaptic health. So there is reason to think they may be helpful. But unfortunately, these success stories have so far only been demonstrated in mouse models or other laboratory experiments. Mice aren't people, and we still await the clinical research to determine their effects on people.

One example is a class of compounds called anthocyanins—a group of antioxidants found in blueberries and other berries—believed to reduce inflammation, decrease oxidative stress, reduce the misfolding of tau proteins, regulate insulin signaling in the brain, and reduce neuroinflammation, all of which can slow cognitive decline and may play a role in Alzheimer's disease prevention and treatment. But clinical data is lacking.

Another potentially beneficial nutrient is quercetin, which belongs to a group of plant pigments called flavonoids. Quercetin is found in apple peels and many other fruits and vegetables. It has been shown to have powerful anti-inflammatory effects, improve mitochondrial metabolic functioning, protect against cell death, and decrease the amount of amyloid and tau pathologies. It makes a lot of sense, but we are still waiting for data in humans.

Polyphenols come in many different forms in a large variety of foods—honey, grape seeds, berries, and many vegetables and legumes—and have many beneficial properties, including prevention of neurodegenerative diseases, but the data is limited to cell culture and animal models.

S-allyl cysteine, an organosulfur compound present in garlic, decreases endoplasmic reticulum (ER) stress, which helps repair misfolded proteins. In mouse models, S-allyl cysteine has been shown to decrease tau pathology, protect against neuron death, decrease inflammation, and protect memory.

The microbiome is of huge interest now, whether it be in our gut or on our skin. The bacteria in our gut can produce a host of beneficial biochemicals as well as harmful ones. Prebiotics are nondigestible components of food that are beneficial to microbiota. Probiotics are live microorganisms. Both are popular nutritional supplements that can regulate and enhance the healthy resident bacteria of our microbiomes. They can enhance synaptic repair and plasticity; decrease inflammation; increase neurotransmitters like serotonin, dopamine, and GABA; as well as have a host of other effects on brain function.

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Within the last 40 years, there has been increasing evidence that lifestyle changes may reverse the progression of coronary heart disease, early-stage prostate cancer, and other chronic conditions. Alzheimer's disease shares some of the underlying biological mechanisms of these diseases—for example, chronic inflammation and oxidative stress. A number of clinical studies are now being conducted to learn about how lifestyle changes—such as diet, stress management, exercise, and directed group support—can slow down, lessen, or reverse the symptoms of Alzheimer's disease. You can contribute to this effort by asking your doctor or social worker if there are trials in your area, and joining as a study participant.

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