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CURRENT RESEARCH ON PREVENTION STRATEGIES

ALZHEIMER'S PREVENTION

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https://www.geneticlifehacks.com/alzheimers-and-apoe-type/

Introduction

Alzheimer's Disease is the most common cause of dementia. Current research points to the cause of the neurodegeneration being a disproportionate inflammatory response resulting in the accumulation of amyloid beta plaque and tau protein tangles. Alongside the excessive inflammatory response is oxidative damage in the brain.[ref]

Prevention is the best strategy, and the initial damage in the brain starts one to two decades before symptoms are apparent. Current drug options for Alzheimer's can delay the progression of the disease, but they are not a cure.

One copy of the APOE E4 allele increases Alzheimer's risk by more than 2-fold, but even without the APOE E4 allele, Alzheimer's prevention is still important. Your overall health is important in Alzheimer's prevention; eating healthy foods, exercising regularly, keeping your brain active, and having good social connections are all basic strategies that everyone should incorporate.[ref]

This guide focuses on what is going on in the brain and specific prevention strategies for each pathway. The overarching picture is one of the specific reasons for increased neuroinflammation — from circadian disruption to plaque formation to an inability to cope with oxidative stress from your body's inflammatory response to pathogens that have reached the brain.

Prevention Strategies at a Glance

Strategy	Evidence / Notes
Block blue light at night	Supports healthy melatonin/circadian rhythm, strongly linked to prevention
Maintain physical activity	Exercise has been shown to lower the risk
Brain energy support	Targeting glucose/prostaglandin-E2 pathways shows promise in mice
Saffron extract (30mg/day)	As effective as standard AD drugs in clinical trials
Low-dose lithium	Epidemiological & clinical trial support for protection
Lemon balm extract	Some evidence for improved cognition in mild/moderate AD
Support liver health (TUDCA)	Neuroprotective bile acids; prevented AD pathology in mouse model
NSAIDs (cautiously)	Population studies show reduced risk; weigh GI/liver risk and genotype
Unprocessed red meat (APOE E4)	Protective for APOE E4 carriers; processed meat increases risk for all
Monitor homocysteine	High homocysteine = higher risk; B-vitamin support helps
Maintain oral hygiene	P. gingivalis & oral microbiome linked to AD risk

Reduce saturated fat (APOE E4)	May help E4 carriers reduce cardiovascular risk
Hormone therapy caution (APOE E4)	HRT increases amyloid beta and tau markers in E4 women
Luteolin, DHA/EPA (fish oil)	Potential neuroprotective effects; fish oil greater benefit in E3 carriers
Minimize alcohol (APOE E4)	Even light/moderate alcohol increases cognitive decline risk in E4
Plasmalogens	Key phospholipid antioxidant; low in AD brains; supplements improve memory
Fibronectin reduction	Excess fibronectin in BBB impairs amyloid-beta clearance
Combined metabolic activators	L-serine, NR, NAC, L-carnitine combination showed cognitive improvements

1. Circadian Rhythm and Melatonin

Number one on the list for preventing Alzheimer's is supporting your circadian rhythm — blocking blue light at night, getting morning sunlight, and optimizing sleep. There is a strong connection between circadian rhythm disruption, melatonin production, immune system regulation, insulin regulation, and healthy brain aging.[ref][ref][ref][ref]

Your body's circadian rhythm is the 24-hour internal molecular clock that drives the timing of many cellular processes — sleeping, wakefulness, meal timing, body temperature changes, cortisol levels, and blood pressure rhythms. Critically, about 40% of the genes active in any cell are impacted by circadian rhythm, and your immune response is strongly tied to your circadian clock.

The core circadian clock genes come in pairs: during the day, BMAL1 and CLOCK tell your cells it is daytime; at night, PER and CRY signal rest and rejuvenation. A key 2018 mouse study showed that BMAL1, a core circadian clock gene, is integral to the daily rhythm of amyloid-beta plaque — disrupting BMAL1 expression in the brain causes increased amyloid plaque deposition and increased APOE expression.[ref] A 2020 study built on this, showing that BMAL1 regulates astrocyte activation; disrupting it increases neuroinflammation and accelerates Alzheimer's pathogenesis.[ref]

A recent study found that light at night from light pollution significantly increases the risk of Alzheimer's, especially at a younger age. The authors concluded that nighttime light was more strongly associated with AD prevalence than alcohol abuse, chronic kidney disease, depression, heart failure, and obesity.[ref]

Melatonin and Amyloid-Beta

Sleeping in complete darkness increases melatonin levels at night. Melatonin production rises in the absence of light in the blue wavelengths. Animal studies clearly show that melatonin is important in reducing amyloid beta levels. Melatonin also acts as an intracellular antioxidant to reduce neuroinflammation.[ref][ref]

Our modern environment with electric lights at night, especially TVs and phones, disrupts our natural circadian rhythm. Blue-blocking glasses worn in the evening for several hours before bed increase natural melatonin production by about 50% in just two weeks.[ref]

Clinical trials are also evaluating the use of melatonin supplements for Alzheimer's.[ref] Additionally, melatonin has been shown to positively reduce any increase in cardiovascular disease risk associated with the APOE E4 allele.[ref]

Lifehacks: Circadian Rhythm and Melatonin

1. Prioritize sleep quality and quantity. Chronic sleep disruption alters the expression of BMAL1 and directly increases symptoms of Alzheimer's.[ref]
2. Sleep in a dark room — no night night lights, no streetlights through the window.
3. Shut off cellphones, tablets, and TV a couple of hours before bedtime. LED screens emit significant blue light, which dysregulates circadian rhythm and decreases melatonin.
4. Get morning sunlight exposure soon after waking to keep your circadian rhythm anchored.

2. Fibronectin, Blood-Brain Barrier, and Amyloid-Beta Plaque

Recently, two large studies examining the interaction of APOE E4 with other genetic variants shed light on how changes in the blood vessels and the blood-brain barrier (BBB) are important for the buildup of amyloid-beta plaques.[ref][ref]

The blood-brain barrier not only keeps bacteria and viruses out of the brain, but also filters many molecules that circulate throughout the body. In Alzheimer's, the buildup of amyloid-beta activates the immune system, causes inflammation, and eventually kills neurons.

In Alzheimer's, there is an increase in fibronectin in the blood-brain barrier.[ref] Fibronectin is best known for its role in forming blood clots, but it is also important in cell adhesion and the BBB. Individuals with the APOE E4 allele do not break down amyloid-beta quite as well as normal for clearance from the brain. The excess fibronectin in the BBB is believed to negatively regulate amyloid-beta clearance.[ref]

In addition, fibronectin changes in the BBB allow more fibrinogen into the brain. Fibrinogen is another clot-forming protein, and decreasing fibrinogen has been shown to help prevent Alzheimer's pathology in animal models.[ref] Genetic variants that decrease fibronectin production have recently been identified as significantly reducing Alzheimer's risk in people with APOE E4.

Lifehacks: Decreasing Fibronectin and Fibrinogen

- Reduce omega-6 oils: Studies show that omega-6 fatty acids increase fibronectin levels.[ref] "Vegetable oils" such as canola, corn, soybean, sunflower, and safflower oils are high in omega-6 fatty acids.
- Vitamin A: Animal studies show that vitamin A deficiency leads to higher serum fibronectin levels.[ref] Vitamin A in the retinol form is important in regulating gene transcription for extracellular matrix genes.[ref]
- Berberine: A natural supplement derived from barberry, goldenseal, and Oregon grape; berberine has been shown in animal models to downregulate fibronectin production.[ref]
- Serrapeptase plus nattokinase: These natural proteolytic enzymes are able to break up fibrinogen. An animal model of Alzheimer's showed that serrapeptase plus nattokinase was effective at reducing brain inflammation and reducing certain Alzheimer's markers.[ref] Note: nattokinase may be contraindicated if you are already on an anticoagulant — check with your doctor.

3. Plasmalogens: A Key to Healthy Brain Aging

Plasmalogens are a unique type of phospholipid and an essential component of cell membranes. In the brain, a specific subtype called ethanolamine plasmalogens is abundant and important in preventing neurodegenerative diseases.

In addition to forming cell membranes, plasmalogens act as phospholipid antioxidants that counteract oxidized lipids. They play a critical role in neutralizing reactive oxygen species (ROS) in the brain — in the presence of ROS, plasmalogens are quickly degraded, so plasmalogen levels may decrease quickly as they neutralize oxidative stress.[ref][ref][ref]

In people with Alzheimer's disease, plasmalogen levels are very low. This appears to be even more pronounced in APOE E4 carriers, who show lower plasmalogen levels, while APOE E2 carriers (a protective genotype) show higher levels.[ref]

Clinical trials in Japan have shown supplemental plasmalogen to be effective at improving memory in people with Alzheimer's. It seems to be more effective if given in mild AD and in younger patients.[ref][ref]

Lifehacks: Boosting Plasmalogens

- Diet: Foods high in plasmalogens include seafood such as mussels, octopus, clams, oysters, squid, scallops, salmon, anchovies, and shrimp.[ref][ref]
- Modified Mediterranean Keto: A ketogenic diet has been shown to improve plasmalogen levels in older adults. A modified Mediterranean keto diet — featuring seafood, lean meats, leafy green vegetables, nuts, berries, and extra virgin olive oil — also showed promising results.[ref]
- Myoinositol: Animal and cell studies show that myoinositol increases brain ethanolamine plasmalogen levels.[ref][ref][ref] It is available as an inexpensive supplement.
- Plasmalogen supplements: Available commercially; study participants used multiple servings daily to see benefits.[ref]

4. Oral Microbiome and Bacterial Translocation

Oral health is also important in preventing Alzheimer's disease. The bacterial species P. gingivalis resides in the mouths of some people and causes gum disease and inflammation. P. gingivalis and other oral species can sometimes enter the bloodstream through bleeding gums — it has been found in the brains of deceased Alzheimer's patients.

Research shows that the oral microbiome is different in people with Alzheimer's compared to healthy controls. A meta-analysis of 16 studies found that the risk of Alzheimer's disease is up to 10-fold higher in people whose brains contain bacteria also found in the oral microbiome.[ref]

This connects to the fibronectin research: a leaky blood-brain barrier could allow oral bacteria to enter the brain in addition to fibrinogen. Oral bacteria in the brain will stimulate an immune response from astrocytes, possibly leading to neuroinflammation and Alzheimer's plaque.[ref][ref]

Lifehacks: Oral Microbiome

5. Practice consistent oral hygiene. Genetic variants in TNF-alpha and other inflammation-related genes can cause excess inflammatory response and bleeding gums — targeting your specific inflammation pathway may help.
6. Consider a water-based flosser (Water Pik or similar). If regular dental floss causes your gums to bleed, oral bacteria will enter your bloodstream regularly.
7. Be cautious with antiseptic mouthwash. Antiseptic mouthwash may alter the oral microbiome and shift the balance toward the wrong types of bacteria. It is also linked to increases in blood pressure due to microbiome changes.[ref] Studies on mouthwash and hospital mortality also raise concerns.[ref]

5. Brain Energy and Cellular Metabolism

Some researchers have dubbed Alzheimer's 'type 3 diabetes' due to changes in how glucose is metabolized in the brain, though it is not a true form of diabetes.

A mouse study investigated metabolic changes in brain cells linked to Alzheimer's and cognitive decline in aging. Researchers showed that energy production is reduced in microglia and macrophages in response to increased prostaglandin E2, an inflammatory signal — causing glucose to be stored as glycogen rather than used for cellular energy. Importantly, inhibiting the EP2 receptor for prostaglandin E2 in myeloid cells reversed cognitive aging in mice.[ref]

Creatine

A 2025 pilot study found that 20g/day of supplemental creatine was well tolerated by patients with Alzheimer's, and the researchers hypothesized that this may increase cognitive performance.[ref]

MCT Oil / Coconut Oil

Medium-chain triglycerides (MCTs) can be used by the brain more easily for energy. A small placebo-controlled clinical trial using coconut oil in elderly adults with mild or moderate dementia showed that 80% of participants had improved or stable cognitive scores, regardless of APOE4 status.[ref]

Combined Metabolic Activators (CMA)

A phase II clinical trial using a combination of four natural supplements showed significant improvements in cognitive scale scores for Alzheimer's patients.[ref] The 'combined metabolic activators' are compounds known to reduce oxidative stress and improve cellular energy in the brain. The CMA contained 12.35g L-serine, 1g nicotinamide riboside, 2.55g N-acetyl-L-cysteine, and 3.73g L-carnitine tartrate.

- L-serine: Supports the glycolytic pathway and synaptic plasticity. In Alzheimer's, the glycolytic pathway is impaired, decreasing serine biosynthesis. Supplementing with l-serine was shown to prevent Alzheimer's behaviors and deficits in animal studies.[ref] Restoring serine levels may prevent damage from altered brain energy in aging.[ref]
- Nicotinamide riboside (NR): A form of vitamin B3 that directly impacts NAD+ levels, which naturally decline with aging. NAD+ is essential for cellular energy production in the mitochondria. Research shows restoring NAD+ levels reduces neuroinflammation.[ref]
- N-acetylcysteine (NAC): A precursor of l-cysteine used by cells to create glutathione, an intracellular antioxidant that stops neuronal damage due to oxidative stress. In Alzheimer's brain culture studies, NAC has been shown to be protective against amyloid-beta plaque formation and cell death in neurons.[ref]
- L-carnitine: Supports mitochondrial energy by transporting long-chain fatty acids into the mitochondria.[ref] It has been shown to mitigate cell damage caused by glycolysis-inhibiting drugs.[ref] Low l-carnitine levels were found in Alzheimer's patients and in early Alzheimer's progression.[ref]

Methylene Blue

Methylene blue (Methylthioninium chloride) has been used in pharmacology for over a century. It can reduce free radical production in the brain mitochondria, and animal studies show good results for Alzheimer's prevention.

Phase III clinical trials using high doses showed no benefits — except in the control groups, which were given low doses of 4–8mg/day.[ref][ref][ref] Multiple animal studies show preventative effects,[ref][ref] but a human randomized, placebo-controlled trial on low-dose methylene blue has not yet been completed. At higher doses, methylene blue can reduce energy production in the mitochondria.[ref] Talk with your doctor about whether low-dose methylene blue is a good option for you.

6. Natural Supplements with Evidence

Saffron

Saffron is a spice and medicinal plant extract used for thousands of years. A 2025 clinical trial found that 30mg/day of saffron extract showed significant improvements in cognitive tests for patients with moderate to severe Alzheimer's disease.[ref] Additional randomized, placebo-controlled clinical trials in mild to moderate Alzheimer's patients show that saffron is as effective as — or more effective than — standard-of-care treatments such as donepezil.[ref][ref]

Low-Dose (Microdose) Lithium

Research shows that the mineral lithium may help prevent Alzheimer's. Lithium is naturally found in food; most people consume up to 3mg/day from dietary sources. Lithium Orotate can be purchased as a mineral supplement in 5mg doses (far lower than lithium carbonate, the prescription medication for bipolar disorder).

Epidemiological studies show that higher lithium levels in drinking water may help protect against dementia. A clinical trial showed that low lithium doses helped Alzheimer's patients have no decrease in cognitive impairment over 15 months.[ref]

Caution: There are interactions between lithium and several prescription drugs. Always check with your doctor or pharmacist before starting any supplement.

TUDCA and Liver / Bile Acid Health

Studies have found altered bile acid metabolites in Alzheimer's brains.[ref][ref] Certain bile acid metabolites are neuroprotective, while others are neurotoxic in the brain.[ref] TUDCA is a supplement that provides neuroprotective bile acids. In a mouse model of hereditary Alzheimer's disease, six months of TUDCA supplementation prevented the Alzheimer's pathology that should have occurred in these mice.[ref] Other studies show that TUDCA prevents cognitive impairment in animal models.[ref]

Resveratrol

For mild to moderate Alzheimer's disease, a small, year-long study using less than 1g/day of resveratrol showed that it attenuated declines in mini-mental status examination (MMSE) scores. Neuroinflammation markers improved significantly.[ref]

Lemon Balm (Melissa officinalis) Extract

A small placebo-controlled clinical trial showed that Melissa officinalis extract actually improved cognitive function in people with mild to moderate Alzheimer's. The study involved 42 Alzheimer's patients.[ref] Lemon balm contains rosmarinic acid, which may affect memory and cognition. It also contains low amounts of harmine, which could help prevent glutamate toxicity.[ref][ref]

Luteolin

Luteolin, a flavonoid found in fruits and vegetables, has been studied for Alzheimer's via reducing neuroinflammation.[ref]

Fish Oil (DHA/EPA)

DHA and EPA are the building blocks for pro-resolving mediators, which are essential in stopping inflammation. Studies on fish oil suggest it may have a greater benefit in protecting against Alzheimer's in people with the APOE E3 allele.

7. Lifestyle Factors

Exercise

Staying physically active has been consistently shown to lower the risk of Alzheimer's.[ref] Research shows that walking, dancing, tennis, weight training, yoga, Zumba, and other forms of exercise can help prevent dementia and keep the brain healthier.

Diet and the Bredesen Protocol

Lifestyle plays a significant role in Alzheimer's risk and timing of onset. Modifying lifestyle and diet has been shown to prevent or delay Alzheimer's disease.[ref]

Dr. Dale Bredesen has developed a comprehensive lifestyle and diet protocol for preventing cognitive decline. A 2024 study showed that the protocol, individualized for the patient, was effective for most in sustaining cognitive improvements.[ref] His book is called The End of Alzheimer's.

Cardiovascular Health and Homocysteine

Several studies have linked cardiovascular health markers to the risk of Alzheimer's. One study showed that an elevated homocysteine level was associated with a higher risk of Alzheimer's.[ref] The best way to know your homocysteine level is to get it tested. Homocysteine levels are often genetically related to MTHFR genes, methylation, and B2, B6, and B12 levels. Carrying the MTHFR variant does not seem to be a risk factor for Alzheimer's unless homocysteine is actually elevated.

NSAIDs

Inflammation in the brain is a key contributor to Alzheimer's pathology. Several studies show that both aspirin and non-aspirin NSAID use reduced the risk of Alzheimer's Disease.[ref][ref][ref] However, you need to weigh the risk of GI and liver damage from long-term NSAID use. Check your CYP2C9 and CYP2C8 genes, as these enzymes are involved in metabolizing some NSAIDs such as ibuprofen.

8. APOE E4-Specific Considerations

The APOE E4 allele is the most significant genetic risk factor for Alzheimer's disease. Many prevention strategies apply broadly, but some have specific importance or adjusted risk-benefit profiles for APOE E4 carriers.

Red Meat Consumption

A 2026 study showed that processed meat consumption (sausages, deli meats) increases Alzheimer's risk slightly for all APOE types. However, high unprocessed red meat consumption decreased Alzheimer's risk significantly in APOE E4 allele carriers (E3/E4 or E4/E4). There was no benefit for APOE E3 or E2 genotypes.[ref] The researchers theorized that the APOE E4 genotype is ancestral to a time before agriculture.

Hormone Replacement Therapy

There are conflicting epidemiological studies on whether hormone replacement therapy is beneficial or detrimental for dementia, and part of the discrepancy may be due to APOE type. A 2025 study involving women in the Wisconsin Registry for Alzheimer's Prevention project found that women with APOE E4 had increased markers for Alzheimer's — including increased amyloid beta and phosphorylated tau — when using HRT. Women without the APOE E4 allele did not show negative effects from HRT.[ref]

Alcohol and Cognitive Decline

A 2014 study found that for older adults carrying the APOE ε4 polymorphism, even light to moderate drinking increased their risk for cognitive decline. Light and moderate alcohol consumption during late life was associated with greater decline in learning and memory among APOE ε4 carriers, while the same pattern was associated with an increase in learning and memory among non-APOE ε4 carriers.[ref]

Saturated Fat and Cholesterol

APOE is a cholesterol transport gene, and there may be an interaction with saturated fat in the diet. While not all studies agree, some point to a diet lower in saturated fat as being helpful for preventing cardiovascular disease in people with APOE E4.[ref] Other studies note that while LDL is slightly higher on average in APOE E4, there is a lower average CRP level, indicating lower inflammation.[ref] The only way to know if your cholesterol is an issue is to test it.

Melatonin and APOE E4

Melatonin has been shown to positively reduce any increase in cardiovascular disease risk associated with the APOE E4 allele, making circadian rhythm optimization particularly important for E4 carriers.

Conclusion: Building Your Prevention Plan

Alzheimer's prevention strategies need to start long before the memory problems begin. The evidence points to several complementary pathways:

- Circadian rhythm optimization keeps the brain in top condition and neuroinflammation under control.
- Healthy plasmalogen levels are essential for combating oxidative stress when it occurs.
- Keeping fibronectin low helps prevent amyloid-beta plaque from forming in the blood-brain barrier.
- Good oral health may help keep bacteria from reaching the bloodstream and the brain.
- Supporting brain energy through diet, exercise, and targeted supplements gives the brain the fuel it needs.
- Lifestyle factors — sleep, exercise, diet, and social connection — remain foundational for everyone.
- APOE E4 carriers should pay special attention to genotype-specific guidance on alcohol, red meat, HRT, and saturated fat.

All of these strategies together may be needed to meaningfully move the needle in preventing neurodegeneration. More research is needed, but in the meantime, you can begin your own prevention plan today using what is currently known.

My Prevention Plan