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How Vitamin A Deficiency Promotes Leaky Gut and Alzheimer's

Analysis by Dr. Joseph Mercola | October 17, 2024

STORY AT-A-GLANCE

- Vitamin A deficiency alters gut microbiome composition, leading to increased intestinal permeability ("leaky gut") and inflammation, contributing to Alzheimer's disease development
- Maintaining optimal vitamin A levels supports gut health, reduces inflammation and slows Alzheimer's progression by preserving cognitive function and reducing amyloid-beta deposition in the brain
- Specific gut bacteria genera, like Eubacterium and Eisenbergiella, are associated with lower Alzheimer's risk, while others like Collinsella and Bacteroides correlate with increased risk
- A healthy gut ecosystem, rich in oxygen-intolerant bacteria producing short-chain fatty acids like butyrate, is crucial for maintaining intestinal barrier function and reducing systemic inflammation
- Probiotics measured in CFUs (Colony-Forming Units) are more reliable than those using AFUs (Active Fluorescent Units), as CFUs only count viable bacteria capable of colonizing the gut

Your gut microbiome plays a crucial role in your overall health, including brain function. Recent research has uncovered a fascinating connection between vitamin A, gut health and Alzheimer's disease risk. A study using mice genetically engineered to develop

Alzheimer's-like symptoms reveals that vitamin A deficiency leads to significant changes in the gut microbiome.[1]

These alterations contribute to increased intestinal permeability, often referred to as "leaky gut," and promote inflammation throughout the body. The researchers found that mice fed a vitamin A-deficient diet had lower diversity in their gut bacteria compared to those receiving adequate or supplemental vitamin A.

Specifically, vitamin A deficiency led to an increase in proinflammatory bacteria like Parabacteroides and Tannerellaceae, while reducing beneficial anti-inflammatory bacteria such as Akkermansia and Verrucomicrobiales. This shift in microbial balance creates an environment that's more conducive to inflammation and contributes to the development of Alzheimer's disease.

Leaky Gut and Inflammation: A Gateway to Alzheimer's?

Your intestinal barrier serves as a critical defense mechanism, preventing harmful substances from entering your bloodstream. The study demonstrated that vitamin A deficiency significantly increased intestinal permeability in the genetically engineered mice. This was evidenced by elevated levels of D-lactate and diamine oxidase in their blood, both indicators of a compromised intestinal barrier.[2]

As a result of this increased permeability, proinflammatory cytokines like TNF-α, IL-1β and IL-6 were found at higher levels in the vitamin A-deficient mice. These inflammatory markers are known to play a role in Alzheimer's disease progression. For instance, TNF-α stimulates the production of amyloid-beta peptides, the primary component of the plaques found in Alzheimer's patients' brains.

IL-1β has been linked to increased brain amyloid-beta deposition, while elevated IL-6 levels are associated with cognitive decline and amyloid-beta aggregation. By maintaining adequate vitamin A levels, you help preserve your intestinal barrier function and reduce systemic inflammation, lowering your risk of developing Alzheimer's disease.[3]

Vitamin A's Impact on Cognition and Amyloid-Beta Pathology

The study's findings highlight the significant impact of vitamin A on cognitive function and Alzheimer's-related brain changes. Mice fed a vitamin A-deficient diet for 12 weeks showed impaired cognition in maze tests compared to those receiving adequate or supplemental vitamin A.[4]

Further, the vitamin A-deficient mice exhibited increased amyloid-beta deposition in their hippocampus, a key brain region involved in memory formation. This suggests that maintaining proper vitamin A levels helps preserve your cognitive abilities and slows the progression of Alzheimer's disease (AD). As noted by bioenergetic researcher Georgi Dinkov:[5]

> *"It took only 12 weeks of vitamin A restriction to establish AD pathology, while the same amount of time supplementing vitamin A was sufficient to produce strong beneficial effects. Crucially, vitamin A restriction elevated biomarkers of gut permeability (D-lactate and DAO), which matches with the post I just did on endotoxin/LPS [lipopolysaccharide] being a major causative factor in AD.*
>
> *Conversely, vitamin A supplementation was effective at restoring the gut barrier, and subsequently preserving cognition even in animals with already established AD."*

In other animal studies, vitamin A deficiency also led to increased production of amyloid-beta peptides and tau phosphorylation — two hallmarks of AD. Interestingly, vitamin A can directly block the production and clumping of amyloid-beta, helping to prevent the formation of harmful plaques in your brain.[6]

Interestingly, while vitamin A supplementation showed benefits compared to deficiency, excessive supplementation (at the upper tolerable intake level) resulted in slightly higher amyloid-beta deposition than the normal intake group.

This underscores the importance of maintaining optimal vitamin A levels without overdoing it. Your body's vitamin A status influences Alzheimer's pathology through

multiple mechanisms, including its effects on gut health, inflammation and direct impacts on brain function.

Optimizing Your Vitamin A Intake for Brain and Gut Health

Given the study's findings, ensuring adequate vitamin A intake supports both gut and brain health. Vitamin A plays essential roles in neuronal plasticity, cognitive function and maintaining immune homeostasis in your intestines. To optimize your vitamin A status, focus on consuming a variety of vitamin A-rich foods.

Good sources include liver, egg yolks, butter from grass fed cows, and orange and yellow vegetables like sweet potatoes and carrots. These foods provide either preformed vitamin A or provitamin A carotenoids that your body can convert to active vitamin A.

While supplementation may be beneficial if you're deficient, it's important not to exceed recommended intake levels, as the study suggests potential negative effects from excessive supplementation. If you're concerned about your vitamin A status, consider having your levels tested before starting any supplementation regimen.

The Role of Vitamins and Minerals in Combating Alzheimer's

While there's no cure yet for Alzheimer's disease, research is uncovering how essential micronutrients help delay its progression. Let's explore how specific vitamins and minerals, beyond vitamin A, could be your allies in maintaining cognitive function and potentially staving off neurodegenerative decline.

Vitamins C and E: Your Antioxidant Shield

Your brain is particularly vulnerable to oxidative stress, which is why antioxidants like vitamins C and E are crucial for cognitive health. Vitamin C, beyond its well-known immune-boosting properties, has shown remarkable effects in animal studies of neurodegenerative diseases.[7]

In Parkinson's disease models, oral vitamin C significantly reduced the loss of dopaminergic neurons and decreased inflammation. For AD, vitamin C's antioxidant effects, combined with vitamin E and selenium, improved synaptic and cognitive functioning.[8] Vitamin E, another powerful antioxidant, has been found at lower levels in the cerebrospinal fluid and serum of AD patients. Studies have shown that higher vitamin E intake is associated with a lower incidence of AD.

In mouse studies, vitamin E deficiency worsened lipid peroxidation and caused amyloid-beta accumulation in the brain, while supplementation increased cholinergic neurotransmission and decreased inflammation. The combination of vitamins C and E creates a potent antioxidant defense for your brain cells, slowing the progression of cognitive decline.[9]

B Vitamins: Your Brain's Metabolic Support Team

The B-complex vitamins also play crucial roles in your brain's health and function. Vitamin B12 deficiency has been linked to an increased risk of developing AD, with lower B12 levels associated with higher levels of inflammatory markers that promote tau hyperphosphorylation and amyloid-beta production. Supplementation with B12 and folate has shown improved cognition and reduced inflammation in AD patients.[10]

Vitamin B6 is essential for neurotransmitter production and homocysteine regulation. While its effects on cognitive decline in healthy older adults may be subtle, B6 deficiency in animal studies has been shown to exacerbate oxidative stress, amyloid-beta deposition and neuronal death.[11]

Vitamin B3 (niacin) is crucial for DNA repair and energy metabolism. In animal studies, niacin supplementation reduced tau phosphorylation and improved cognitive performance. Vitamin B1 (thiamin) is vital for glucose metabolism in your brain. Thiamin deficiency has been linked to increased amyloid-beta production, while supplementation has shown promise in delaying cognitive decline in AD patients.[12]

Minerals: The Unsung Heroes of Brain Health

While vitamins often take the spotlight, minerals play equally important roles in your brain health. Iron, for instance, is crucial for oxygen transport and neurotransmitter production. However, **iron overload** leads to oxidative stress and inflammation in the brain. An imbalance of iron in your body can lead to ferroptosis, a programmed cell death pathway known to play a role in neurodegenerative diseases like Alzheimer's.[13]

Zinc, however, is essential for numerous enzymes and plays a role in neurotransmitter release. Zinc deficiency has been linked to cognitive decline, while proper levels help protect against amyloid-beta toxicity.[14]

Selenium, another important mineral, has shown neuroprotective effects in animal studies, potentially through its antioxidant properties. Magnesium is involved in numerous biochemical reactions in your brain, and increased dietary intake has been associated with a decreased incidence of cognitive impairment.[15]

It's worth noting that imbalances in these minerals can also affect your gut health, leading to leaky gut. By maintaining proper mineral balance, you're not only supporting your brain health directly but also indirectly by promoting a healthy gut-brain axis.

More Ways Your Gut Microbes Influence Alzheimer's Risk

A study analyzed genetic data from thousands of people to identify specific gut microbes that help protect against or **increase vulnerability to Alzheimer's**.[16] The researchers found that the abundance of certain bacterial genera in the gut was genetically linked to Alzheimer's diagnosis.

Specifically, higher levels of bacteria like Eubacterium, Eisenbergiella and Prevotella were associated with lower Alzheimer's risk. On the flip side, greater amounts of Collinsella, Bacteroides and Veillonella correlated with increased risk. These findings provide some of the strongest evidence yet that your gut microbiome composition plays a role in brain health and cognitive decline as you age.

While more research is needed, this study opens up exciting possibilities for using gut bacteria analysis or probiotic therapies as part of Alzheimer's prevention and treatment strategies in the future.

Butyrate-Producing Bacteria Protect Your Brain

Several of the bacterial genera found to be protective against Alzheimer's in this study are known to produce butyrate, an important short-chain fatty acid (SCFA).[17] Butyrate has anti-inflammatory properties and helps maintain the integrity of your gut lining. The researchers identified Eubacterium, Eisenbergiella and related bacteria as potentially beneficial. These microbes metabolize dietary carbohydrates into butyrate in your colon.

By reducing inflammation and supporting gut barrier function, butyrate-producing bacteria help prevent harmful substances from entering your bloodstream and affecting your brain. This adds to a growing body of evidence suggesting that nurturing beneficial gut bacteria through your diet and lifestyle support cognitive health.

Inflammation-Promoting Bacteria Linked to Higher Alzheimer's Risk

On the other hand, some of the bacterial genera associated with increased Alzheimer's risk in this study are known to have proinflammatory effects.[18] For example, Collinsella was identified as a particularly significant risk factor. Previous research has found higher levels of Collinsella in the guts of people with inflammatory conditions like rheumatoid arthritis.

This genus increases the production of inflammatory compounds and reduces the expression of proteins that maintain a healthy gut barrier. Similarly, some Bacteroides species secrete lipopolysaccharide (LPS), an inflammatory molecule that contributes to dysfunction of the gut lining and neuroinflammation.[19]

By promoting chronic low-grade inflammation, these types of bacteria increase vulnerability to neurodegenerative processes over time, highlighting the complex

interplay between your gut microbiome, systemic inflammation and brain health.

Intriguingly, this study also uncovered connections between gut bacteria and known genetic risk factors for Alzheimer's disease. The researchers found that the abundance of certain bacterial genera was correlated with variants in the APOE gene, one of the strongest genetic risk factors for late-onset Alzheimer's.[20]

For instance, people carrying the high-risk APOE ε4 allele tended to have higher levels of Collinsella. This suggests there may be interactions between your genetic predisposition and the composition of your gut microbiome that influence Alzheimer's risk.

While more research is needed to understand these relationships, the findings point to the gut microbiome as a potential avenue for personalized prevention strategies. In the future, it may be possible to tailor dietary and probiotic approaches based on both genetic risk factors and gut bacteria profiles to optimize brain health as you age.

AFU vs CFU: The Probiotic Measurement Controversy

Navigating the world of probiotics can be overwhelming, especially when faced with countless options, each claiming to be the best. You may have come across probiotics boasting high colony-forming units (CFUs). It's a common belief that the higher the CFU count, the better the probiotic. However, I want to shed some light on this misconception and help you understand what truly makes a high-quality probiotic supplement.

CFUs are indeed a unit of measurement used to determine the number of viable bacterial cells in a probiotic. When you browse the shelves at your local health store, you'll notice a wide range of CFU counts, with some supplements advertising numbers as high as 100 billion or more. It's easy to assume that these sky-high CFU counts are the ultimate indicator of a superior product, but that's not the whole story.

While CFUs are important, they are just one piece of the puzzle. A probiotic's effectiveness depends on several factors, including the specific bacterial strains used, the delivery mechanism, and the existence of clinical studies supporting its efficacy.

Let's take a closer look at how CFUs are measured. In a microbiology lab, a bacterial culture is added to an agar plate, and after a few days, the colonies that grow are counted. However, it's crucial to understand that not all these colonies will survive the journey through your digestive system. Many probiotic bacteria are sensitive to stomach acid and bile, which means that a significant portion of the CFUs you swallow may not even reach your gut alive.

As if all this wasn't already confusing enough, we have a new variable to contend with. You may have noticed that some probiotic companies use AFU (Active Fluorescent Units) instead of the more traditional CFU (Colony-Forming Units) to measure the bacteria in their products. I want to shed some light on why this practice can be misleading and potentially detrimental to your health goals.

When you're looking for a probiotic to support your gut health, you want to ensure that you're getting a product filled with live, active bacteria that can colonize your gut and provide the benefits you're seeking.

This is where the CFU measurement comes in. CFU is the gold standard in the industry, counting only the viable bacteria that can grow, multiply, and form colonies within your digestive system. It's a direct reflection of the bacterial cells that are alive and ready to work their magic. The National Institutes of Health (NIH) recommends buying only probiotics that list the CFU at the end of the product's shelf life.[21]

Now, let's talk about AFU. While AFU offers a more rapid assessment of bacterial populations compared to traditional CFU methods, it presents significant limitations in accurately determining probiotic potency. Unlike CFU, which exclusively counts viable bacteria capable of forming colonies, AFU detects a broader spectrum of cells, including those that may be injured, non-viable, or even dead.

This overestimation can mislead consumers and healthcare professionals about a product's actual probiotic content. Additionally, the reliance on fluorescence for bacterial detection can introduce variability and potential inaccuracies in the final count. Consequently, AFU might not be the most reliable indicator of a probiotic's efficacy.

You might be wondering why a company would choose to use AFU instead of CFU. Unfortunately, the answer often lies in marketing. Higher numbers look more impressive on the label, making the product appear more potent and effective than it really is. However, those dead or inactive bacteria won't do anything for your gut health. They're just taking up space in the capsule, and you're not getting the full value of what you've paid for.

This is a significant issue in the supplement industry, as it can mislead consumers who are trying to make informed decisions about their health. Regulatory bodies such as the FDA and EFSA recognize CFU as the standard measurement for probiotics, so when a company deviates from this norm, it's essential to question their motives and be cautious.

If you come across a probiotic using only AFU count, don't be afraid to ask questions. A reputable company should be transparent about their labeling and willing to explain what these numbers mean. They should ensure that you, as the consumer, understand the difference between AFU and CFU and how it impacts the product's effectiveness.

At the end of the day, using AFU instead of CFU can inflate the perceived potency of a probiotic, leading you to believe you're getting more than you are. It's crucial for companies to be honest and clear in their labeling, so you can make an informed decision and get the most bang for your buck.

As you continue your journey to better gut health, remember to look for probiotics that use CFU as their primary measurement. If a company isn't being transparent about their labeling or relies heavily on AFU, it might be time to look for a more trustworthy product that prioritizes your well-being over marketing tactics.

Although complex carbs and foods with fiber nourish these bacteria you need to be very careful about using them until you have increased your cellular energy. This is because most people have far more dangerous disease-causing bacteria and the same food that nourishes Akkermansia will nourish the disease-causing bacteria. This will increase endotoxin and cause you to get sick.

In my new book, "Your Guide to Cellular Health," which comes out in October, I review a green, yellow, red, classification system of carbs. Green are carbs like white rice and dextrose that nearly everyone can tolerate as they are absorbed in the upper intestine and do not stimulate endotoxin production.

Red carbs are typically what are considered some of the healthiest food. However, they have fibers that need to be avoided by most unless they have a pristine gut that has very low pathogenic bacteria.

Maintaining a Healthy Gut Ecosystem Is Key to Brain Health

A flourishing gut ecosystem is home to a diverse array of microorganisms that work in harmony to protect your health. Nurturing beneficial oxygen-intolerant bacteria, including crucial species like Akkermansia, strengthens your intestinal defenses and fosters an environment that promotes overall wellness. This ties directly to the findings discussed earlier, where certain bacterial genera were found to be protective against Alzheimer's disease.

These beneficial bacteria ferment dietary fibers to produce SCFAs, particularly butyrate. As mentioned, butyrate-producing bacteria like Eubacterium and Eisenbergiella were associated with lower Alzheimer's risk. Butyrate nourishes your colonic epithelial cells, reinforcing the intestinal barrier. SCFAs also stimulate mucin production, creating a protective shield against harmful bacteria.

A reduction in oxygen-intolerant bacteria leads to increased intestinal permeability, or leaky gut. This allows toxins, undigested food particles and harmful microbes to enter your bloodstream, triggering systemic inflammation and chronic health issues.

Oxygen-intolerant bacteria are vital for converting indigestible plant fibers into beneficial fats. They thrive in an oxygen-free environment, which requires adequate cellular energy to maintain. However, factors like **seed oil consumption**, exposure to **endocrine-disrupting chemicals** (EDCs) in plastics and electromagnetic fields (EMFs) impair this energy production, making it difficult to sustain the ideal no-oxygen gut environment.

Moreover, a leading cause of death is, in my view, endotoxemia resulting in septic shock. This occurs when you secrete endotoxin from facultative anaerobes, also known as oxygen-tolerant bacteria, which shouldn't be in your gut. These pathogenic bacteria produce a highly virulent form of endotoxin, or LPS, which can cause inflammation if they cross your compromised gut barrier into systemic circulation.

Thus, leaky gut or a disturbed microbiome is one of the fundamental causes of all disease, including neurodegenerative conditions like Alzheimer's. **Improving mitochondrial function** and **maintaining a healthy gut ecosystem** promote beneficial bacteria growth while reducing harmful endotoxin effects, helping to mitigate factors contributing to dementia and other chronic diseases.

Further, as the featured study suggests, by maintaining optimal vitamin A levels, you also help support a healthy gut microbiome, reduce inflammation and lower your risk of cognitive decline and Alzheimer's disease.

Sources and References

- [1, 2, 3, 4] Front. Nutr., 26 March 2024
- [5] To Extract Knowledge from Matter August 25, 2024 (Archived)
- [6, 7, 8, 9, 10, 11, 12, 14, 15] Brain Disorders June 2024, Volume 14, 100139
- [13] Science Advances April 19, 2023, Introduction
- [16, 17, 18, 19, 20] Scientific Reports March 31, 2023
- [21] Office of Dietary Supplements. Probiotics: What You Need to Know. National Institutes of Health. Updated June 2023