Medical Research Archives

European Society of Medicine

OPEN ACCESS

Published: April 30, 2024

Citation: Newport, M., T., 2024. Ketogenic strategies for Alzheimer's disease and other memory impairments: History, rationale, and 288 caregiver case reports. Medical Research Archives, [online] 12(4). https://doi.org/10.18103/mra.v12i4.5316

DOI: https://doi.org/10.18103/mra.v12i4.5316

ISSN: 2375-1924

CASE REPORT

Ketogenic strategies for Alzheimer's disease and other memory impairments: History, rationale, and 288 caregiver case reports

Mary T. Newport, M.D

Spring Hill Neonatology, Inc. 15500 Serengeti Blvd. Spring Hill, Florida, USA.

preemiedoctor@aol.com or marytnewportmd@gmail.com

ABSTRACT

Glucose hypometabolism predates Alzheimer's disease symptoms by at least one to two decades. Ketones are an alternative fuel to glucose and are taken up normally in affected regions of the Alzheimer's brain and could address certain pathologies that are common in the aging brain and exaggerated in Alzheimer's disease including insulin resistance, a brain-energy deficit, mitochondrial dysfunction, oxidative stress, and neuroinflammation. Ketones have also been shown to reduce formation of beta-amyloid plaques and neurofibrillary tangles in animal models. Experts have estimated that at least 30 percent of Alzheimer's and other dementias could be avoided by adopting a healthy diet, increasing physical activity, and correcting other modifiable lifestyle risk factors. Mild to moderate ketosis can be achieved through consumption of a healthy whole food low-carbohydrate ketogenic diet, ketogenic oils containing medium-chain triglycerides, or exogenous ketone supplements as well as intermittent or overnight fasting, and moderately vigorous aerobic exercise. An analysis was performed of 288 anecdotal reports about people with Alzheimer's, other dementias, Parkinson's disease with dementia, mild cognitive impairment, and other diagnosed or subjective memory impairments consuming coconut oil and/or medium-chain triglyceride oil. Improvement was reported by 89.2 percent, no improvement by 7.3 percent, and no improvement but stabilization for at least 3 months by 2.4 percent. One or more improvements were reported in the areas of memory/cognition (65.3%), social/behavior/ mood/personality (32.6%), speech/language/conversation (33%), resumption of self-care/other activities (24.7%), physical symptoms (18.4%), sleep (3.5%), appetite (2.4%), vision (1.4%), and improvement that was otherwise unspecified (8%). Certain fatty acids found in medium-chain triglyceride oil and coconut oil are ketogenic but also have other important biological effects which, along with polyphenols and other bioactive substances in virgin coconut oil, could explain these results. Adopting a personalized ketogenic lifestyle plan using one or more ketogenic strategies could address certain pathological processes that occur in the aging brain while potentially improving symptoms in people with Alzheimer's disease. In addition, this approach could possibly prevent or delay the onset of cognitive impairment during aging, though larger long-term studies would be needed to confirm this.

Introduction

Since the 1990s, Alzheimer's disease (AD) research has largely focused on targeting beta-amyloid plaques and neurofibrillary tangles, which were first described in 1906 by Dr. Alois Alzheimer in the brain of Auguste Deter who died with young onset dementia. Clinical trials of more than forty drugs have reported reducing beta-amyloid plaques in the brain but none have reported significant sustained improvements in cognition or other symptoms, and some have worsened or even accelerated the disease process. Recent developments in brain imaging have revealed that the beta-amyloid plaque burden can be substantial in cognitively healthy elderly adults and minimal in some people with AD[1]. None of the drugs currently approved by the FDA for AD, mostly cholinesterase inhibitors that increase availability of acetylcholine, lead to meaningful improvement in cognition or functionality beyond slowing the disease progress for up to six months. Beta-amyloid is now known to be antimicrobial against many different pathogens[2,3] and removing it could have adverse consequences since numerous studies have implicated various microbes as possible causes or contributors to AD[4].

Ketogenic therapies address certain metabolic derangements that can occur in the aging brain but are exaggerated in the Alzheimer's brain, including glucose hypometabolism, a brain energy deficit, mitochondrial dysfunction, oxidative stress, and neuroinflammation. These conditions are also present in certain other dementias, in people with Parkinson's disease (PD), in some people with MCI, and in certain other neurodegenerative and psychiatric disorders[5,6].

In 1921, endocrinologist Dr. Russell Wilder was the first to report that a very high fat diet with moderate protein and minimal carbohydrate mimicked the high ketone levels found during prolonged fasting, a treatment for epileptic seizures, and that this "ketogenic diet" (KD) successfully eliminated or reduced seizures in people with drug-resistant epilepsy[7]. More recently, KD has become the treatment of choice for glucose transporter 1 (GLUT 1) deficiency syndrome and pyruvate dehydrogenase complex deficiency (PDCD) syndrome. Less strict versions of the diet have also shown efficacy for epilepsy, including the medium-chain triglyceride (MCT) oil modified ketogenic diet, the modified Atkins diet, and the low-glycemic index diet[8].

Clinical trials of KD have reported encouraging results for people with Alzheimer's, Parkinson's, and other neurodegenerative, neurological, and psychiatric disorders as well as for obesity, migraines, congestive heart failure, recovery from myocardial infarction, and as an adjunct to standard-of-care treatment for various malignancies[9,10,11]. Clinical trials of a well-formulated KD in people with type 2 diabetes have reported normalization of glucose control parameters along with weight loss, better blood pressure control, and improved lipid profile[12,13]. Case studies of people with insulin resistance and mild Alzheimer's disease have reported similar metabolic improvements along with a marked increase in Mini-Mental State Examination scores from 21-23 to 28-29 of 30 points[14,15]. In 2019, the American Diabetes Association published new guidelines that recognized the improved glucose control that has been reported in numerous studies of low-carbohydrate and

ketogenic diets in people with diabetes[16]. Extreme carbohydrate restriction extended the lives of people with type 1 diabetes, sometimes for years, before insulin as a therapeutic was available in 1921 and the ketogenic diet has enjoyed a resurgence in interest while allowing better glucose control and reduction in insulin requirement in people with type 1 diabetes[17].

The idea of using exogenous ketones as a therapeutic for AD and other disorders of insulin resistance with glucose hypometabolism originated with Richard L. Veech, M.D., D. Phil. of the National Institutes of Health in the 1990s. In 1997, Veech and his associates completed experiments in which working rat hearts were perfused with a solution containing glucose to which they added insulin or starvation levels of the ketones betahydroxybutyrate (BHB) and acetoacetate (AcAc), or a combination of insulin and ketones. The addition of either insulin or ketones increased the efficiency of the heart by about 25 percent, and the combination of insulin and ketone bodies increased the efficiency by about 36 percent, indicating that the hearts pumped more efficiently using less oxygen when ketones were available. Furthermore, ketone bodies duplicated nearly all the acute effects of insulin[18,19]. In 2000, Veech and associates reported results of a study in which cultured rat hippocampal neurons were subjected to beta-amyloid Aß1-42 (an AD model) or rat dopaminergic mesencephalic neurons were subjected to 1-methyl-4-phenylpyridinium (a PD model). The cultures were incubated with either a control medium or BHB at a millimolar level found during prolonged starvation. The cultures incubated with BHB showed increased neuronal survival, larger neuronal size, and more outgrowths of neurites than in control cultures, thereby providing neuroprotection[20].

Also in 2000, Samuel Henderson, PhD proposed that tricaprylic acid (C8:0), a medium-chain triglyceride (MCT) oil which is partly converted to ketones in the liver, might provide a level of ketosis that might improve memory and cognition in people with AD. A phase 2 single-dose pilot study was conducted in which participants with AD received a drink called AC-1202 with 40 grams of the MCT oil or a placebo drink at two separate visits. There was significant improvement in MMSE scores in 9 of 20 people, specifically in the subset who were apolipoprotein E4 (ApoE4)-. Subsequent randomized controlled trails (RCTs) of 152 people with mild to moderate AD and 159 people with age-associated memory impairment receiving either 20 grams MCT daily or a placebo for 90 days reported rapid and sustained cognitive improvement on various tests which was again most apparent in ApoE4$^-$ subjects[21]. ApoE4 positivity occurs in about 25% of the general population but 40% of people with AD.

Between 2000 and 2004, Veech and associates wrote several hypothesis papers on the potential therapeutic benefits of ketones for people with neurodegenerative diseases and other disorders and developed the (R)-3-hydroxybutyl (R)-3-hydroxybutyrate ketone monoester[22,23,24,25]. Veech and others have also reported that ketones have a direct effect on the hallmark pathologies of AD. In a study by Kashiwaya et al, compared to controls, 3xTgAD mice consuming the ketone monoester had significantly less accumulation of beta-amyloid plaques and neurofibrillary

tau tangles and reduced anxiety[26]. In another series of studies by Wu et al, the same ketone monoester reduced Aß 42 accumulation, attenuated microglial activation, improved mitochondrial respiration in hippocampal neurons, and improved cognitive function in FXFAD mice. Furthermore, using RNA sequencing, the study showed that "BHB-regulated genes mainly annotated in aging, immune system, nervous system, and neurodegenerative diseases"[27]. In an *in vitro* study, Yin et al found that incubation of neurons with a mixture of BHB and AcAc prevented perforation of neurons by beta-amyloid and suppressed intracellular Ab42 accumulation which rescued mitochondrial complex I activity, reduced oxidative stress, and improved synaptic plasticity. The same group also found that administration of BHB and AcAc to an APP mouse model for two months significantly reduced amyloid burden and greatly improved learning and memory[28]. In addition, ketones can reduce neuroinflammation by acting as antioxidants and scavengers of free radicals, by inhibiting activation of the NLRP3 inflammasome, and through other anti-inflammatory and immunomodulatory mechanisms[29,30,31,32].

Since 2004, many human clinical trials have variously reported improvement in memory and cognition, physical symptoms, physical strength, self-care, and/or biomarkers of AD in people with AD, mild cognitive impairment, and PD with classic ketogenic diet, modified Mediterranean ketogenic diet, ketogenic diet with MCT oil, as well as consuming CO or MCT oil with the habitual diet. Several recent review articles have summarized the results of many of these studies[5,33,34,35,36,37]. Separate studies have reported improvement in cognitive and other symptoms, when compared to a low-fat control diet, in people with PD and AD consuming a ketogenic diet with coconut oil in nearly all diet program recipes (found in the report supplementary material)[38,39]. A program of walking on a treadmill three times a week in people with mild Alzheimer's was found to nearly triple ketone uptake in the brain[40]. Consumption of MCT oil by frail elderly people in Japan improved not only cognition on various tests but also increased grip strength and speed of walking, and improved scores on a leg open-and-close test, and significantly increased expiratory flow volumes[41,42,43]. An RCT of 65 people with MCI taking placebo versus a C8:0/C10:0 MCT oil 15 gm twice daily for six months reported improvement in the MCT group in multiple cognitive domains and also confirmed an increase in brain energy from ketones after consuming MCT oil using dual tracer PET imaging in a subset of participants[44]. This study also reported uptake of ketones in white matter and in the dorsal attention network that correlated with improvements in processing speed[45,46] and the study also found a reduction in plasma cardiometabolic and inflammatory biomarkers[47]. However, this study did not find a difference between $ApoE4^{+}$ and $ApoE4^{-}$ people[44]. Interestingly, a recent study of 84 people receiving 15 gm twice daily of either coconut oil (CO) or canola oil reported improvement on average only in the people receiving CO who were $ApoE4^{+}$[48], the opposite of the Costantini et al studies.[21] A study of ketone response to CO and MCT oils alone or in various ratios showed that AcAc levels were higher than BHB levels when

taking just CO but were the reverse when taking just MCT oil[49], which might explain the difference.

KETONES ARE AN ALTERNATIVE FUEL TO GLUCOSE FOR THE BRAIN AND CAN BYPASS INSULIN RESISTANCE

As explained in the many hypothesis and review papers already cited, cells require fuel to produce adenosine triphosphate (ATP) to carry out basic and complex functions. When consuming a typical high-carbohydrate diet, glucose serves as the predominant fuel for the brain and other organs. Ketones are a primitive fuel used by single-cell and very complex organisms like humans and, unlike glucose, ketones do not require insulin directly or indirectly to enter the brain and other organs, cells, or mitochondria. Ketones are produced endogenously during prolonged fasting, starvation, or while consuming a ketogenic diet after liver glucose stores are depleted leading to release from adipose tissue of long-chain fatty acids, which can be used by most organs as fuel but do not readily cross the blood brain barrier. Some fatty acids are converted mainly in the liver to the ketone acetoacetate (AcAc), which can be further metabolized bidirectionally to betahydroxybutyrate (BHB), the main circulating ketone, and to acetone, which is thought to be mostly exhaled. Acetone is volatile and difficult to measure in blood; however, about 37% of acetoacetate is converted to acetone. Therefore, acetone levels can be quite high and could contribute to brain energy or have other metabolic contributions that have not yet been discovered[50]. Ketones are small molecules that are readily taken up by the brain using monocarboxylate transporters and can be converted to acetyl CoA which directly enters the tricarboxylic acid (TCA) cycle to produce more ATP molecules than an equivalent amount of glucose. Ketones can be used as fuel by all organs, except the liver where ketones are generated from fatty acids. Thus, ketones address metabolic disorders at a very fundamental level, which explains a seeming panacea effect.

Glucose hypometabolism is an early feature of AD and may be present decades before the onset of symptoms, and even in young at-risk ApoE4$^+$ adults[51,52]. Insulin resistance[53,54], GLUT1 and GLUT 3 deficiencies[55], and PDH Complex 1 deficiencies[56] impede glucose entry into the brain, into neurons and glia, and into mitochondria resulting in abnormal glucose uptake in the areas affected by AD. Using dual tracer ketone (acetoacetate) and glucose PET imaging in more than 300 young and older adults, Stephen Cunnane and associates have identified a brain-energy deficit in cognitively healthy older adults (7 to 9%) that worsens in people with mild cognitive impairment (MCI) ($\geq$10%) and is accelerated in people with mild AD ($\geq$20%). However, ketones are taken up in both gray and white matter brain regions affected by abnormal glucose uptake in MCI and AD[45,46,57]. As discussed previously, neuroinflammation with activation of microglia is another prominent feature of AD that could be ameliorated by ketogenic therapies.

RESPONSES OF 288 PEOPLE WITH ALZHEIMER'S DISEASE OR OTHER MEMORY IMPAIRMENT TO COCONUT OIL AND/OR MEDIUM-CHAIN TRIGLYCERIDE OIL

The following study focuses on the effects of CO and MCT oil in people with Alzheimer's, dementia or other memory impairment and

was presented by the author in-person as a poster and a brief online video following acceptance through a peer-reviewed process at the Alzheimer's Association International Conference in Amsterdam on July 18, 2023.

Methods:

OVERVIEW: An analysis of a large collection of anecdotal reports about people with AD, dementia, and other types of memory impairment was performed to determine response or non-response and types of improvements reported while consuming coconut oil (CO) and/or MCT oil.

SUBJECTS: The subjects of the analysis include the index case (the author's husband) and a subset of unsolicited reports about 359 other individuals received by the author from late-2008 to mid-2014 about individuals consuming coconut oil and/or MCT oil. The analysis included people with Alzheimer's, another type of dementia specified or unspecified, Parkinson's disease with dementia or memory impairment, mild cognitive impairment, other memory impairment related to a diagnosed disorder, and subjective memory complaints. Reports about 72 individuals were excluded from the analysis because the diagnosis or complaint did not include a diagnosis of memory impairment or subjective memory complaint, or the person was not consuming coconut oil or MCT oil. Reports on a total of 288 individuals met the criteria and were included in the analysis. Most reports were received by email and occasionally provided by standard mail or verbally and were mainly provided by family caregivers, or occasionally by the affected person or a paid caregiver. If the report was vague, the person was asked to provide greater detail, if possible, but respondents were not otherwise prompted regarding what improvements might be expected. The original copies of the reports have been retained.

TABULATION OF RESULTS: All reports about a specific individual were assigned a unique number beginning with "001" for identification purposes. Using the corresponding number, information derived from the reports for each individual was entered on an Excel spreadsheet including age, gender, diagnosis or memory complaint, concurrent medications for AD or dementia, use of CO and/or MCT oil, or an MCT medical food, along with all verbatim comments pertaining to the person's symptoms and observations of improvements, lack of improvement, and/or apparent side effects while consuming the oils. The data from the Excel spreadsheet were tabulated manually on a separate document according to the number and percent of people who reported improvement, no improvement, or no improvement but stabilization for at least three months as well as for each category of improvement reported. Verbatim phrases from the reports (shown on Table 1) were used to categorize the types of improvements reported, which included improvements related to "memory and cognition", "social interaction, behavior, and mood", "speech, conversation, verbal skills", "resumption of self-care and other activities" such as work, cooking, or hobbies, "physical symptoms", "sleep", "appetite", and "vision". Each set of reports was read and re-read at least three times to ensure that all pertinent information was retrieved. The tabulation and summations

of the data were triple checked to ensure accuracy. Since this was a collection of spontaneously provided anecdotal reports which were not solicited for a formal study and anonymity has been maintained, prior IRB approval was not feasible.

Table 1. Verbatim phrases from 288 anecdotal reports to categorize the types of improvements reported. The table is from poster presentation P3-582 by the author Mary T. Newport, M.D. at the Alzheimer's Association International Conference on 18 July, 2024 in Amsterdam, The Netherlands, entitled, "Reports of Responses to Coconut Oil and Medium-Chain Triglyceride (MCT) Oil in 288 Persons with Alzheimer's and Other Memory Impairment."

PHRASES IN REPORTS USED TO CATEGORIZE IMPROVEMENTS OF 288 PEOPLE WITH ALZHEIMER'S, DEMENTIA, OR OTHER MEMORY IMPAIRMENT IN RESPONSE TO COCONUT OIL AND/OR MEDIUM-CHAIN TRIGLYCERIDE (MCT) OIL				
IMPROVED MEMORY/COGNITION	**IMPROVED SOCIAL INTERACTION/ BEHAVIOR/ MOOD**	**IMPROVED SPEECH/ CONVERSATION/ VERBAL SKILLS**	**RESUMED SELF CARE/ OTHER ACTIVITIES**	**IMPROVED PHYSICAL SYMPTOMS**
Higher scores on memory or cognitive test	More interaction with others	Speaking again	Showering again without help	Less tremor
Improved clock drawing	Better sense of humor	Clearer speech	Taking care of self again	Getting out of bed without help
Better cognition	Less agitation and/or anxiety	Less repetitiveness	Doing things around the house	Able to walk again
Better sense of direction	Improved behavior	Making sense	Doing household chores again	Walking without assistance
Improved reading comprehension	Less hostile	More logical	Preparing meals again	Improved strength
Reading again	Less aggressive	Improved conversation	Resumed a hobby	More ambulatory
Able to do mental math again	Happy	More talkative	More functional	More energy
Able to write again	Improved mood	Improved verbal skills		Less stiffness
More awareness of time/place	Less depression	Better word recall		Improved balance
Recognizing people or places	Feels better	Expressing thoughts		Less dizziness
Less distractible	**IMPROVED SLEEP**	**IMPROVED APPETITE**	**IMPROVED VISION**	Fewer episodes of faintness, clamminess, sweating
More alert	Fewer nightmares	Improved appetite	Visual disturbance gone	Improved gait
Brighter	Sleeping better		Able to see more clearly	Fewer episodes seizure/twitching
Improved awareness	No longer sleeping excessively sleep			Pain relief
	Stopped twitching during sleep			

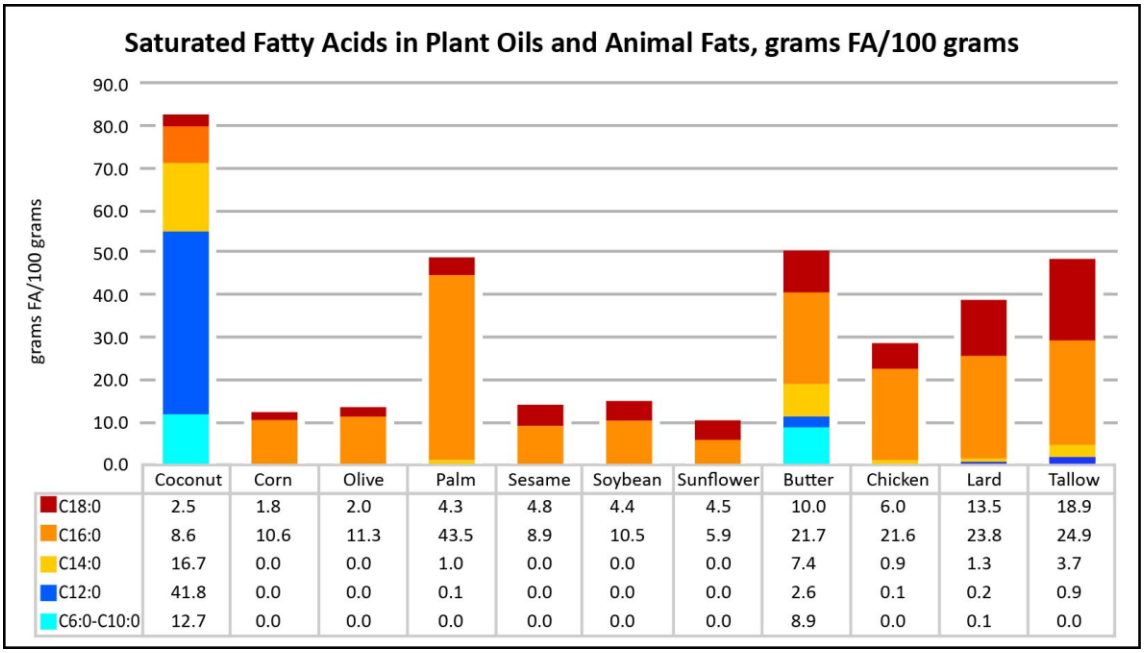
Results:

The index case SJN was the husband of the author whose response first to coconut and MCT oil and later in a pilot study of the Veech ketone monoester was previously reported in detail with SJNs permission in a peer-reviewed journal[58]. SJN was an ApoE $4^{+}/3^{+}$ male who worked as an accountant, and was diagnosed at age 54 with early onset-AD after onset of memory symptoms at age 51. SJN was 58 years old and at FAST stage 5-6 at the time of the dietary intervention. SJN also had facial and intention tremors, a stiff slow gait, and occasional hallucinations. SJN was consuming a whole food diet and taking DHA supplements for about two years prior to the intervention but had continued to worsen significantly during that time.

The intervention with coconut oil (CO) in May 2008 was inspired by a press release on the positive study results of the AC-1202 MCT oil discussed above. The rationale was explained

in US patent application (20080009467) which also stated that MCT oil is extracted from CO or palm [kernel] oil. CO is the richest natural source of medium-chain fatty acids (MCFAs), which are 6- to 12-carbons long and comprise about 55% of the total fat. Most of the saturated fatty acids in CO are the MCFAs (C6:0 to C12:0) and myristic acid (C14:0). CO contains about 11% of total fats as the long-chain fatty acids palmitic and stearic acid, which is in the same range (about 11 to 14%) as other commonly consumed vegetable oils that contain virtually no fatty acids with 14 or fewer carbons (Table 2). Palm kernel oil has a similar composition to CO but about 5-7% fewer MCFAs[59]. CO was more widely available in the US in 2008 than MCT oil, and 35 gm was used as the initial intervention for SJN to approximate the 20-gm test dose of AC-1202.

Table 2. About 55% of the fatty acids in coconut oil (CO) are medium chain with 6 to 12 carbons (C6:0 to C10:0, light blue; C12:0, medium blue) which, along with myristic acid (C14:0, light orange), are not found in most other commonly consumed vegetable oils or animal fats apart from the milk fat of humans and other mammals. CO contains about the same amount of long-chain saturated fats (dark orange and red) as most other commonly consumed vegetable oils like corn, olive, soybean, and sunflower oils and much less than in animal fats. In addition, CO contains no cholesterol. The table with graph is from poster presentation P3-582 by the author Mary T. Newport, M.D. at the Alzheimer's Association International Conference on 18 July, 2024 in Amsterdam, The Netherlands, entitled, "Reports of Responses to Coconut Oil and Medium-Chain Triglyceride (MCT) Oil in 288 Persons with Alzheimer's and Other Memory Impairment."



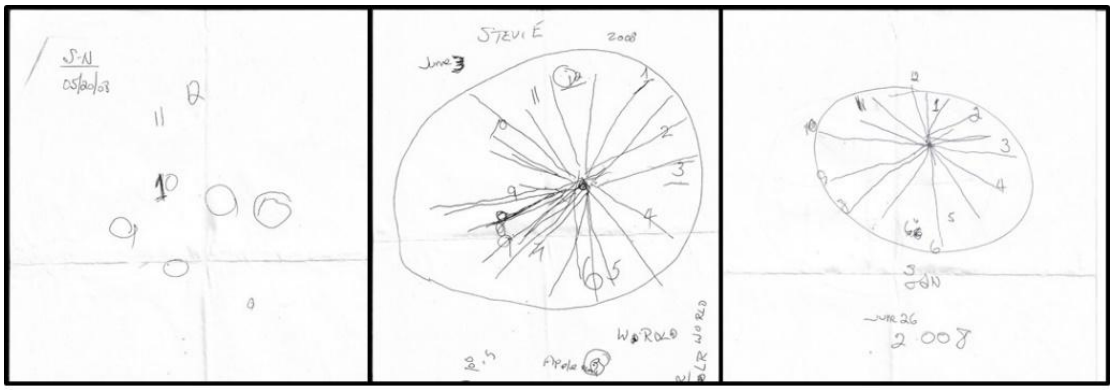
	Coconut	Corn	Olive	Palm	Sesame	Soybean	Sunflower	Butter	Chicken	Lard	Tallow
C18:0	2.5	1.8	2.0	4.3	4.8	4.4	4.5	10.0	6.0	13.5	18.9
C16:0	8.6	10.6	11.3	43.5	8.9	10.5	5.9	21.7	21.6	23.8	24.9
C14:0	16.7	0.0	0.0	1.0	0.0	0.0	0.0	7.4	0.9	1.3	3.7
C12:0	41.8	0.0	0.0	0.1	0.0	0.0	0.0	2.6	0.1	0.2	0.9
C6:0-C10:0	12.7	0.0	0.0	0.0	0.0	0.0	0.0	8.9	0.0	0.1	0.0

SJNs scores on the MMSE in drug trial screenings on successive days improved from 14 (1 day before) to 18 of 30 about 4 hours after taking the first serving of CO 35 gm and increased to 20 of 30 about two months later at another clinical trial screening. SJN continued to receive CO 35 gm with breakfast and additional CO with the other meals

beginning on day 2. At about six weeks, SJN began to receive a 4:3 mixture of MCT/coconut oil, which was increased gradually over about two months to 135-165 ml per day in four servings while reducing other fats and carbohydrates.

SJN reported that "the light bulb came on" in his brain the day he started taking CO. During the first days to weeks, SJN became more talkative and animated, his personality and sense of humor returned, along with whistling, joking, finding appropriate eating utensils; his intention tremor resolved within 20-30 minutes of taking coconut oil, and the facial tremor resolved completely. Between one and two months, SJN recognized family members again and participated in conversation, he could tie his own shoes again, his stiff gait completely normalized, he could run again, and he was able to resume yard and housework. Meanwhile, SJNs clock drawing improved dramatically at days 14 and 37 (Figure 1).

Figure 1. Clock drawings by SJN the day before starting the coconut oil intervention while screening for a clinical trial and then at 14 and 37 days after starting coconut oil. The original drawings in this figure were scanned and previously included in poster presentation P3-582 by the author Mary T. Newport, M.D. at the Alzheimer's Association International Conference on 18 July, 2024 in Amsterdam, The Netherlands, entitled, "Reports of Responses to Coconut Oil and Medium-Chain Triglyceride (MCT) Oil in 288 Persons with Alzheimer's and Other Memory Impairment."



1 Day Before Coconut Oil **14 Days on Coconut Oil** **37 Days On Coconut Oil**

By 4 months after starting coconut oil, SJNs visual disturbance resolved (described by SJN as "words moving around like pixels on the page like satellite break up") and he could read again. By 9 months, SJN's reading comprehension and delayed recall improved. SJN began to work as a hospital volunteer, and he appeared to stabilize.

About 2 months after starting CO, SJN was accepted into a semagacestat clinical trial, and it was later revealed that he was on placebo for 18 months. During the first year in the trial (about 14 months after starting coconut), SJN had improved by 6 of 75 points on the Alzheimer's Disease Assessment Scale-Cognitive and by 14 of 78 points on the Activities of Daily Living test. At the time of his early-onset AD diagnosis in 2004, SJNs MRI was reported as "Normal" but, just before entry into the semagacestat trial in June 2008,

his MRI was reported as "Diffuse involutional changes of frontal and parietal lobes and moderate left-sided and severe right-sided atrophy of amygdala and hippocampus, consistent with AD". Nearly 2 years after starting coconut oil in April 2010, his MRI was reported as "Stable MRI brain in comparison to prior [2008] examination."

Within six weeks of crossing over from placebo to semagacestat in early 2010, SJN suffered a serious setback with worsening and new AD symptoms, poor wound healing, fainting, and elevated CPK enzymes, and he discontinued participation in the trial. About two months later, under the guidance of Dr. Richard L. Veech, SJN began a pilot study (n=1) of the ketone monoester (R)-3-hydroxybutyl (R)-3-hydroxybutyrate averaging 20 gm of ketone monoester three times daily. Within 2 hours of the first dose, SJN could speak and write the alphabet again, and by 24 hours, SJN could once again shower, shave, and dress himself without assistance; his mood, affect, abstract thinking, and insight improved, and the new symptoms resolved within six weeks. SJN was stable for another 20 months and altogether enjoyed nearly four better-quality years after starting ketogenic oils until sustaining a fall with a head injury resulting from a prolonged generalized seizure with apnea and cyanosis. SJN became completely dependent thereafter and passed away from AD on January 2, 2016. SJN donated his brain which showed "advanced pathological stage AD (Braak 6) and Lewy bodies, amygdala predominant".

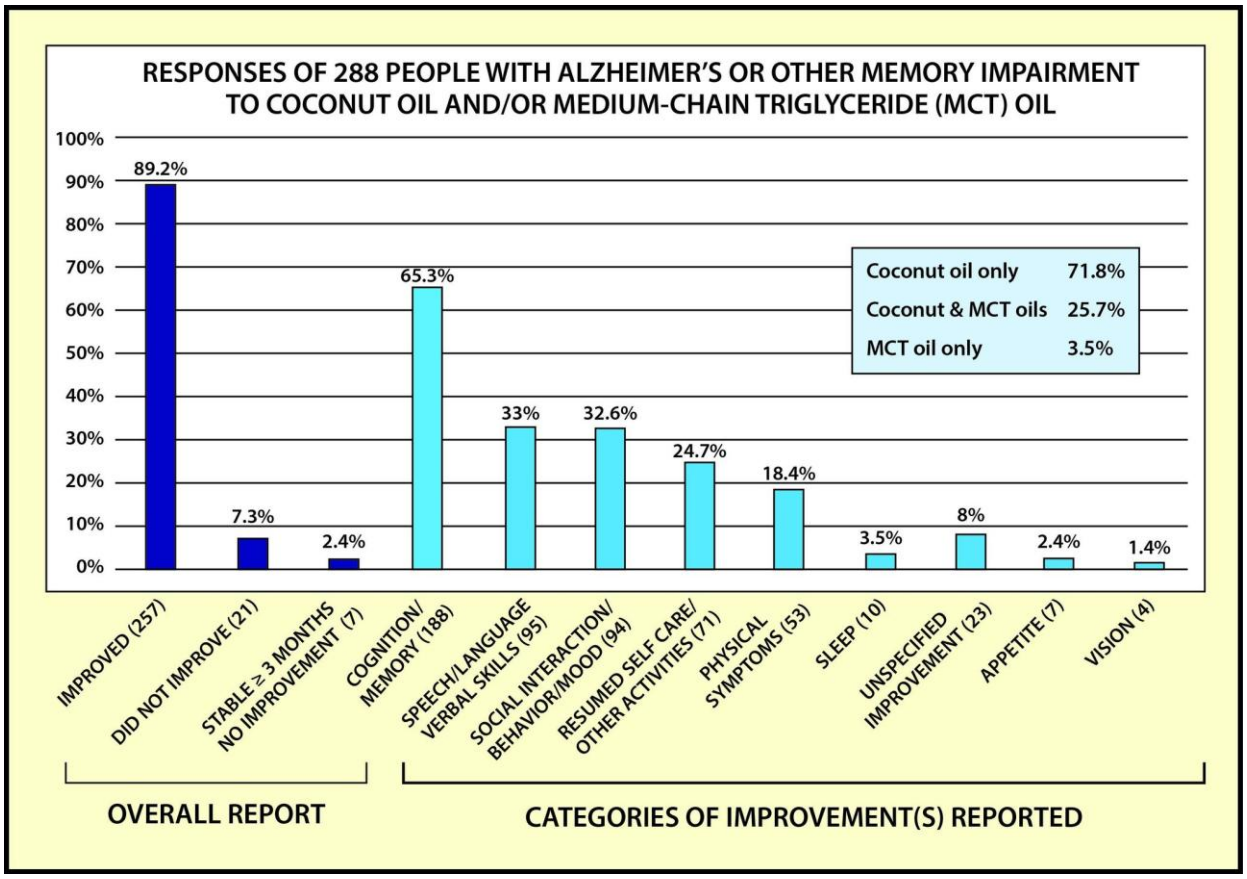
In July 2008, the author self-published a white paper on the scientific basis of ketogenic strategies for AD, SJN's response to ketogenic oils, and the urgent need for studies of the oils and Veech's ketone ester (https://coconutketones.com/wp-content/uploads/2016/09/whatifcure.pdf) Thereafter, from late-2008 to mid-2014, the author received emails, letters, and a few telephone calls, mostly from caregivers but sometimes from the affected person, with anecdotal reports on 359 other individuals, mainly adults with Alzheimer's, dementia, or other memory impairment or complaint but also children, teens, and adults affected by PD, autism, amyotrophic lateral sclerosis, bipolar disorder, strokes, hypoxic events, accidents, or other conditions without reported memory impairment. Many people provided just one communication whereas some maintained contact for months to years. The analysis here was limited to the 288 people reported to have memory impairments including AD, dementia, MCI, PD with memory impairment, or other diagnosed or subjective memory complaints (Table 3).

Table 3. Demographic information derived from anecdotal reports of 288 people with Alzheimer's disease (AD) and other disorders with memory impairment. This figure is from poster presentation P3-582 by the author Mary T. Newport, M.D. at the Alzheimer's Association International Conference on 18 July, 2024 in Amsterdam, The Netherlands, entitled, "Reports of Responses to Coconut Oil and Medium-Chain Triglyceride (MCT) Oil in 288 Persons with Alzheimer's and Other Memory Impairment." AD = Alzheimer's disease, FTD = frontotemporal lobe dementia, CBD = Corticobasal dementia, PCA = posterior cortical atrophy, TBI = traumatic brain injury, PSP = posterior supranuclear palsy

DEMOGRAPHIC INFORMATION	
Age range	33 to 94 years
Gender	51.4% F - 47.6% M - 1% not reported
Memory complaint	55.9% Alzheimer's 9.4% Other dementia, specified* 15.3% Other dementia, not specified 5.9% Parkinson's with AD/other memory impairment 2.4% Mild cognitive impairment 11.8% Subjective complaint without diagnosis 13.5% Memory complaint with other diagnosis**
*Dementia diagnosis (of 288): Vascular (8), FTD (6), CBD (6), Lewy body (5), PCA (2) ** Diabetes (5), stroke (5), ALS (5), Huntington's (3), Multiple sclerosis (3), Epilepsy (3), bipolar (3), autism (2), gen. dystonia (2), coma (1), TBI (1), PSP (1), hypertension (1), cancer (1), Prader Willi (1), migraine (1), peripheral neuropathy (1) **Note:** Some people had more than one diagnosis	

Of the 288 subjects, 72% consumed only CO, 26% CO plus MCT oil, and 2% MCT oil only. The amount of oil consumed varied widely from person to person. People who requested guidance were advised to begin with ½ to 1 teaspoon of the oil two or three times per day with meals and to increase very slowly to at least 2 to 4 tablespoons daily if tolerated. 89.2% reported improvements overall, 7.3% no improvement, 2.4% no improvement but stabilization for at least 3 months. Most people reported more than one type of improvement in the areas of memory/ cognition (65.3%), social/behavior/ mood/ personality (32.6%), speech/ language/ conversation (33%), resumption of self-care/ other activities (24.7%), physical symptoms (18.4%), and sleep (3.5%), appetite (2.4%), vision (1.4%), and "improved" but otherwise unspecified (8%) (Figure 2). Fewer than 10% of people reported an upset stomach or diarrhea when starting CO or MCT oil. Otherwise, no adverse effects were reported.

Figure 2. Overall response and types of improvements reported in 288 people with Alzheimer's disease and other disorders with memory impairment. This figure is from poster presentation P3-582 by the author Mary T. Newport, M.D. at the Alzheimer's Association International Conference on 18 July, 2024 in Amsterdam, The Netherlands, entitled, "Reports of Responses to Coconut Oil and Medium-Chain Triglyceride (MCT) Oil in 288 Persons with Alzheimer's and Other Memory Impairment."



Limitations:

One important limitation of this study is that people might be more likely to contact the author if they had experienced a positive response, although some people reported that there was no response whatsoever. While guidance on how much CO or MCT to consume was provided, many people did not report how much they consumed in an average day, therefore it was not possible to determine reliably the range of CO and/or MCT oil that were consumed. In addition, the author was not the medical provider of the subjects and was unable to confirm diagnoses of the persons reporting their responses to CO and MCT oil or perform any testing.

Discussion:

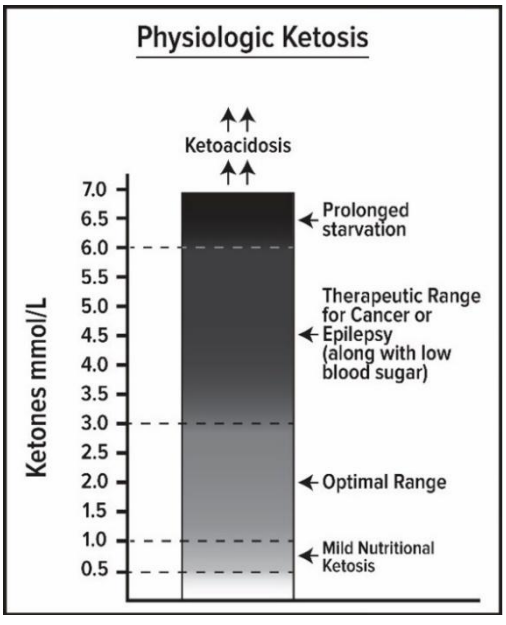
A PERSONALIZED PLAN BASED ON KETOGENIC STRATEGIES COULD REDUCE THE RISK OF ALZHEIMER'S DISEASE AND DEMENTIA

Modifiable lifestyle risk factors have been identified that account for a substantial portion of dementia cases with poor diet at the top of the list. Making certain lifestyle changes could delay or prevent cognitive decline such as adopting a healthier diet, increasing physical

activity, controlling blood glucose and blood pressure, smoking cessation, avoiding excessive alcohol intake, correcting hearing and vision impairments, getting adequate sleep, treating sleep apnea, and avoiding social isolation[60]. Adopting a ketogenic lifestyle could also address several of these risk factors.

"Nutritional ketosis" is generally defined as an increase in blood ketone levels within the physiological range of about 0.3 to 6.0 millimoles per liter (mmol/L) and can be achieved through intermittent fasting, consumption of a ketogenic diet (KD), ketogenic oils, such as CO and MCT oil, and/or exogenous ketone supplements.[61,62] Higher ketone levels are generally recommended for people with drug-resistant epilepsy, rare metabolic syndromes such as GLUT1 or PHD Complex 1 deficiency syndromes, or as an adjunct to standard-of-care treatments for certain cancers. Ketone levels increase after about 10 to 12 hours of fasting and continue to increase for as long as fasting is maintained. Consuming water or other sugar-free/calorie-free liquids during a fast with or without added fat such as CO or heavy cream in coffee or tea do not usually interfere with ketosis. A KD can be tailored to the individual through manipulation of the ratio of grams of fat to combined grams of protein and carbohydrate; ketosis will generally occur if protein is kept at a moderate level (about 1 to 1.5 gm/kg/day) and fewer than 50-60 grams of carbohydrates are consumed daily, with the remaining energy requirement consumed as fat. Generally, the higher the ratio, the higher the ketone levels will become, and therefore, the KD is a spectrum of diets within the physiological range (Figure 3).

Figure 3. The ketogenic diet is not just one diet but rather a spectrum of diets with combined physiological levels of betahydroxybutyrate and acetoacetate of 0.3 to 6 mmol/L. Ketone levels tend to fluctuate throughout the day, but generally the higher the grams of fat intake compared to grams of protein and carbohydrate combined, the higher the ketone level will become. Improvement in cognition and/or other symptoms has been reported in people with AD, MCI, and other disorders at ketone levels as low as 0.3 to 1.0 mmol. This figure is from poster presentation P2-651 by the author Mary T. Newport, M.D. at the Alzheimer's Association International Conference on 17 July, 2024 in Amsterdam, The Netherlands, entitled, "Personalized Nutritional Ketosis Through Whole-Food Low-Carb Diet, Medium-Chain Triglycerides, and Other Ketogenic Strategies for People with Mild Cognitive Impairment and Alzheimer's Disease."



Clinical trials and case studies of CO, MCT oil, and ketogenic diets have reported improvement in cognition and symptoms of

AD and MCI with ketone levels as low as 0.3 to 1.0 mmol/L. Exogenous ketone supplements, such as ketone salts, ketone esters, and mixtures of salts and esters can increase betahydroxybutyrate (BHB) levels substantially higher than CO or MCT oil for several hours. Ketone salts are generally comprised of BHB bound to sodium, potassium, calcium, and/or magnesium, and currently available esters in the US combine BHB or C8:0 with R 1,3-butanediol, which is metabolized mainly in the liver to more BHB and is also available separately as a supplement in the US.

People who do not tolerate coconut or MCT oil can still achieve ketosis by consuming a ketogenic diet, exogenous ketone supplements, exercise, and/or intermittent fasting. Ketogenic strategies can be used alone or in combination to devise a personalized plan to improve overall metabolic health or to address a specific metabolic disorder (Figure 4).

Figure 4. Ketogenic strategies result in the typical increases in ketone levels shown on the figure, though the response can be quite variable between individuals and at different times of day and can be affected by what a person consumes and when. Ketone levels resulting from ketogenic strategies are considerably lower than levels that occur in diabetic ketoacidosis (DKA), which occurs when blood glucose is markedly elevated and there is no insulin available. Taking an excessive amount of a ketone ester could result in transient ketoacidosis but this is not the same as DKA. This figure is from poster presentation P2-651 by the author Mary T. Newport, M.D. at the Alzheimer's Association International Conference on 17 July, 2024 in Amsterdam, The Netherlands, entitled, "Personalized Nutritional Ketosis Through Whole-Food Low-Carb Diet, Medium-Chain Triglycerides, and Other Ketogenic Strategies for People with Mild Cognitive Impairment and Alzheimer's Disease."

KETOGENIC STRATEGY:	KETONE LEVELS mmol/L:
Caffeine	0.2 to 0.3
Coconut Oil	0.3 to 0.5
Vigorous Exercise	0.3 to 0.5
Overnight Fast	0.3 to 0.5
MCT Oil	0.3 to 1.0
Branched Chain Amino Acids	0.3 to 1.0
Ketone Mineral Salts	0.5 to 1.0
Classic Ketogenic Diet	2 to 6
Starvation	2 to 7
Ketone Esters (Oral or IV)	2 to 7 or higher
Diabetic Ketoacidosis	10 to 25

COCONUT OIL AND MEDIUM-CHAIN TRIGLYCERIDE OIL CONTAIN BIOACTIVE SUBSTANCES THAT APPEAR TO BE BENEFICIAL IN ALZHEIMER'S DISEASE

Medium-chain fatty acids (MCFAs) found in CO and in medium-chain triglyceride (MCT) oil are partly converted to ketones in the liver regardless of what else is consumed, though may be less ketogenic if consumed with a high carbohydrate meal. The remaining MCFAs are used as fuel and not stored as fat. MCT oil has been used since the 1960s to treat infants, children, and adults with malnutrition and malabsorption disorders and has been used to preserve or increase muscle mass and strength due to its effect on protein metabolism and to aid in fat reduction due to its thermogenic properties[63]. In the late 1970s to mid-1980s, MCT oil was added to the feedings of extremely premature newborns since it was well absorbed and enhanced growth. Then infant formula manufacturers developed special formulas for premature newborns and babies with gastrointestinal conditions containing MCT oil[64]. MCFAs are

about 10 to 17% of the fats found in human milk, predominantly lauric acid (C12:0)[65], and nearly all commercial infant formulas since the mid-1980s contain CO or palm kernel oil and sometimes MCT oil to supply the MCFAs found in human milk. C12:0 and myristic acid (C14:0), which is also prominent in CO but not found much in other oils and fats with the exception of milk fat, are found in colostrum and amniotic fluid, which the fetus ingests, and therefore, the fatty acids likely have a role in growth, development, and metabolism though the exact roles are not yet clear[66]. The breastfed newborn is naturally in ketosis and ketones are known to provide the building blocks for lipids in the lipid- and cholesterol-rich brain[67].

MCFAs with chain lengths up to at least 10 carbons cross the blood brain barrier and can be used directly as fuel by brain cells[68,69]. Caproic acid (C6:0) and caprylic acid (C8:0) are highly and rapidly ketogenic. Capric acid (C10:0) has delayed conversion to ketones compared to C8:0, but C10:0 also has anticonvulsant activity with efficacy comparable to valproic acid and stimulates mitochondrial biogenesis[68]. It is uncertain whether lauric acid (C12:0) crosses the blood brain barrier and ketone production is even more delayed than for C10:0. However, a study by Nonaka et al found that C12:0 remains elevated in the blood at higher levels and for a longer duration than the shorter MCFAs and potently stimulates production of ketones in mouse astrocytes in cultures[70]. If this effect is confirmed *in vivo,* this would suggest a more direct effect of C12:0 in the brain.

Improvement in AD symptoms from consuming CO and MCT oil is usually attributed to generation of ATP by circulating ketones, and ketosis likely does explain the relatively acute improvement in cognitive and physical symptoms that some people report. However, other biological properties of ketones, fatty acids, and other substances in coconut oil could explain the longer-term improvements reported in this study. As previously mentioned, ketones have antioxidant, anti-inflammatory, and neurodegenerative disease-modifying effects. C12:0, which is about half of the fat in CO, is highly antimicrobial to herpes simplex and other viruses with a lipid capsule, microbes that cause dental decay, the Borrelia Burgdorferi spirochete that causes Lyme disease, yeast, fungi, and other pathogens that have been implicated in numerous studies as possible causes or contributors to AD[71,72,73,74]. C12:0 is used for its antimicrobial properties in medical and veterinary applications, oral and skin care products, and in household disinfectants[75]. C12:0 is about 7% of the lipids in human milk and is reported to protect the newborn from infection[76].

Several other recent studies of the effects of medium-chain fatty acids, including C12:0, on the brain have been reported:

- Middle-aged and older people in Italy were less likely to have cognitive impairment who had moderate consumption of MCTs, especially C12:0, and short-chain fatty acids (SCFA, 4 or fewer carbons), which are found in milk fat, butter, ghee, and fermented foods and are also produced by bacteria in the gut from fiber in whole foods. Also, people with lower blood levels of acylcarnitines containing MCFAs, including C12:0, and the SCFA 2-hydroxybutyric acid were more likely to have AD and a lower volume of pre-frontal gray matter[77].

- Another group reported that fatty acids of 10 to 14 carbons, significantly stimulated the degradation of exogenous human Aβ40 peptides by directly increasing the activity of insulin degrading enzyme (IDE), which is involved in the breakdown and removal of beta-amyloid plaques from the brain, whereas long-chain fatty acids (C16 and C18) had essentially no effect, and very long-chain saturated fatty acids (C20:0 to C24:0) had the opposite effect. The authors suggested that CO "might be beneficial in preventing or treating Alzheimer's disease" due to its enrichment with MCFAs, including C12:0, and C14:0[78].
- Hyperactivated microglia in AD and other neurodegenerative conditions are associated with neuroinflammation in AD and release nitric oxide and proinflammatory cytokines thereby promoting the other neuropathologies that occur. A series of experiments using activated microglia found that C12:0 suppressed production of nitric oxide and pro-inflammatory cytokines, and suppressed phagocytosis, all of which would be expected to reduce subsequent neuronal damage "in AD patients who consume coconut oil"[79].
- Ischemic stroke is worsened by the occurrence of a sudden increase in blood glucose which produces toxic glucose metabolites resulting in poor utilization of glucose as an energy source and oxidative stress, particularly in the microvasculature of the brain. This leads to the demise of endothelial cells and loss of tight junctions resulting in an increased volume of damage in the surrounding tissues and a subsequent decline in cognitive and motor functions. A set of experiments using a stroke mouse model found that, in the presence of elevated blood glucose, C12:0 attenuated the volume of the infarct by reducing brain edema and endothelial cell death, by enhancing the diameter of blood vessels, by promoting vascular angiogenesis, and by stabilizing barrier functions; there was also a significant reduction in 4-HNE-positive vessels, which is a marker of lipid peroxidation. Therefore, "lauric acid administration provides neuroprotection to the microvascular endothelial cell by limiting oxidative stress-induced damage to the tight junctions"[80].

Virgin CO also contains polyphenols with antioxidant and anti-inflammatory properties, such as caffeic acid, p-coumaric acid, ferulic acid, methyl catechin, dihydrokaempferol, gallic acid, quercetin and myricetin glycoside and other substances that inhibit amyloid plaque formation[81,82,83,84].

Blood ketones from CO are lower than from an equivalent amount of MCT oil, since CO contains about 10-15% of the more ketogenic C8:0 and C10:0 fatty acids found in standard MCT oils, and therefore, much more CO would be required to achieve the same peak levels as MCT oil. However, the ketone levels from MCT oil, especially pure C8:0, peak much sooner at about 90-120 minutes and return to baseline more quickly than CO. The fatty acids in CO are metabolized to ketones much more slowly, first C8:0, then C10:0, and later C12:0, which is about half of the CO fats, and therefore, consuming CO could allow for a more sustained availability of ketones. SJN began with CO and later received a mixture of CO and MCT oil in a 4:3 ratio to try to increase peak ketone levels while providing a sustained level of mild ketosis as well as to

provide the other beneficial substances like C12:0 and polyphenols found in virgin CO.

DOES COCONUT OIL REALLY INCREASE SERUM CHOLESTEROL LEVELS?

A common concern is whether adding CO to the diet will increase serum cholesterol levels, particularly low-density lipoprotein cholesterol (LDL-C). Many dietary studies comparing the effects of edible oils on the lipid profile have used CO to represent saturated fat. However, as previously mentioned, most of the saturated fatty acids in CO are the MCFAs (C6:0 to C12:0) and myristic acid (C14:0), which are not found in most other commonly consumed vegetable oils but are present in milk fat (Table 2).

Dietary fat studies since 1985 comparing oils have generally arrived at conclusions based on the differences in lipid profile response between saturated and unsaturated fats and oils rather than considering the actual results for the people consuming individual oils. Results were reported in this way, for example, in a recent systematic review and meta-analysis of sixteen studies which concluded that "coconut oil increases LDL-cholesterol"[85-98]. However, when the actual results were considered for the coconut oil groups separately, 6 of the 16 studies reported a decrease in LDL-C[88,90,92,93,96,97,] and a study of 96 people who had a history of serious cardiac events and concurrent statin use reported an insignificant 0.8% increase in LDL-C in response to consuming CO for two years[87]. All but one of the sixteen studies[93] reported an increase in high-density lipoprotein cholesterol (HDL-C). In addition, four studies reported average increases in LDL-C of +0.09 to 0.66 mmol/L in people consuming polyunsaturated oils (soybean, peanut, and sunflower)[86,87,88,91]. These results suggest that the long-held belief that "coconut oil increases cholesterol" is incorrect. Standard deviations for results were quite large (as high as 1.2 mmol/L) in many of the studies for CO as well as for other oils, which suggests that some individuals may experience an increase, decrease, or no change in lipid values in response to consuming a new oil.

Most relevant to this report, the study by Fernando et al of 43 people with AD consuming 15 gm twice daily of virgin coconut oil for 21 days reported significant average decreases from baseline values for total and LDL-C that were greater for the people who were ApoE4^{+} than ApoE4^{-}, and there was a similar increase in HDL cholesterol for both groups. In addition, a systematic review and meta-analysis of studies using MCT oil by McKenzie et al found no significant effect on blood total, LDL, or HDL cholesterol levels[99], as did the six-month study of 65 people with MCI conducted by Fortier et al discussed previously[44].

Conclusions:

Just a few targeted FDA-approved drug therapies claim to temporarily slow cognitive decline. However, nutritional ketosis broadly addresses important pathological changes in the AD and aging brain, including insulin resistance, glucose hypometabolism, mitochondrial dysfunction, oxidative stress, and inflammation. A growing number of RCTs of ketogenic diet, MCT oil, CO, and other ketogenic strategies reporting positive outcomes add weight to this study of anecdotal reports, which are generally considered less compelling than large

randomized controlled trials (RCTs). However, a collection of 288 anecdotes about people consuming CO and/or MCT oil with 89 percent reporting meaningful improvements in cognition, social interaction, self-care, and other areas important to daily life warrants attention and could stimulate interest in conducting larger clinical trials.

RCTs for treatments for AD and MCI generally include assessments for memory and other cognitive impairments, and sometimes include assessments of activities of daily living and depression but often do not include evaluations for improvement in physical symptoms, behavioral and other mood, visual, sleep, and appetite disturbances, which are other common symptoms of AD that affect quality of life for the affected person and family, especially the caregivers. When evaluating a potential treatment for AD and other neurological and psychiatric conditions, consideration should be given to evaluating the effects on these other important aspects of daily life. In addition, the purpose of an RCT is to determine not only efficacy but whether there are toxicities or other serious adverse effects related to an intervention, usually a drug. Most drugs for AD have failed trials due to lack of efficacy and/or serious adverse effects. Nutritional ketosis is a food-based intervention, and studies of ketogenic diet, CO, and MCT oil have reported few, if any, serious adverse effects. Studies of exogenous ketones are currently in progress. Coconut and its oil have been consumed by many millions in the tropical areas of the world for millennia. CO and sometimes MCT oil have been used in commercial infant formulas worldwide since the 1980s to provide the MCFAs found in human milk. CO and MCT oil are considered safe for newborns, are foods, and not potentially dangerous drugs. It seems reasonable to inform people and their caregivers who are dealing with Alzheimer's, Parkinson's, and disorders with memory and other cognitive impairments about the potential for ketogenic oils, ketogenic diet, and other ketogenic strategies to improve symptoms so that they at least have the option to try this approach. In addition, adopting a personalized ketogenic lifestyle plan could possibly prevent or delay the onset of cognitive impairment during aging, though long-term studies would be needed to confirm this.

Conflict of Interest Stattement:

The author declares that there is no conflict of interest, and no payment was received for carrying out this study or for preparation of the manuscript.

Funding:

None.

Acknowledgements:

None. The study and manuscript are the sole work of the author.

References:

1. Espay AJ, Sturchio A, Schneider LS, Ezzat K. Soluble Amyloid-β Consumption in Alzheimer's Disease. *J Alzheimers Dis.* 2021;82(4):1403-1415. doi: 10.3233/JAD-210415.

2. Soscia SJ, Kirby JE, Washicosky KJ, Tucker SM, Ingelsson M, Hyman B, Burton MA, Goldstein LE, Duong S, Tanzi RE, Moir RD. The Alzheimer's disease-associated amyloid beta-protein is an antimicrobial peptide. *PLoS One.* 2010;5(3):e9505. doi: 10.1371/journal.pone.0009505.

3. Kumar DK, Eimer WA, Tanzi RE, Moir RD. Alzheimer's disease: the potential therapeutic role of the natural antibiotic amyloid-β peptide. *Neurodegener Dis Manag.* 2016;6(5):345-8. doi: 10.2217/nmt-2016-0035.

4. Itzhaki RF, Lathe R, Balin BJ, et al. Microbes and Alzheimer's Disease. *J Alzheimers Dis.* 2016;51(4):979-84. doi: 10.3233/JAD-160152.

5. Cunnane SC, Trushina E, Morland C, et al. Brain energy rescue: an emerging therapeutic concept for neurodegenerative disorders of ageing. *Nat Rev Drug Discov.* 2020 Sep;19(9):609-633. doi: 10.1038/s41573-020-0072-x.

6. Palmer CM, Gilbert-Jaramillo J, Westman EC. The ketogenic diet and remission of psychotic symptoms in schizophrenia: Two case studies. *Schizophr Res.* 2019;208:439-440. doi: 10.1016/j.schres.2019.03.019.

7. Höhn S, Dozières-Puyravel B, Auvin S. History of dietary treatment from Wilder's hypothesis to the first open studies in the 1920s. *Epilepsy Behav.* 2019;101(Pt A):106588. doi: 10.1016/j.yebeh.2019.106588.

8. Kossoff EH, Zupec-Kania BA, Auvin S, et al. Optimal clinical management of children receiving dietary therapies for epilepsy: Updated recommendations of the International Ketogenic Diet Study Group. *Epilepsia Open.* 2018;3(2):175-192. doi: 10.1002/epi4.12225.

9. Dyńka D, Kowalcze K, Paziewska A. The Role of Ketogenic Diet in the Treatment of Neurological Diseases. *Nutrients.* 2022;14(23):5003. doi: 10.3390/nu14235003.

10. Weber DD, Aminzadeh-Gohari S, Tulipan J, Catalano L, Feichtinger RG, Kofler B. Ketogenic diet in the treatment of cancer - Where do we stand? *Mol Metab.* 2020;33:102-121. doi: 10.1016/j.molmet.2019.06.026.

11. Dyńka D, Kowalcze K, Charuta A, Paziewska A. The Ketogenic Diet and Cardiovascular Diseases. *Nutrients.* 2023;15(15):3368. doi: 10.3390/nu15153368.

12. Feinman RD, Pogozelski WK, Astrup A, et al. Dietary carbohydrate restriction as the first approach in diabetes management: critical review and evidence base. *Nutrition.* 2015;31(1):1-13. doi: 10.1016/j.nut.2014.06.011.

13. Hallberg SJ, McKenzie AL, Williams PT, et al. Effectiveness and Safety of a Novel Care Model for the Management of Type 2 Diabetes at 1 Year: An Open-Label, Non-Randomized, Controlled Study. *Diabetes Ther.* 2018;9(2):583-612. doi: 10.1007/s13300-018-0373-9.

14. Stoykovich S, Gibas K. *APOE* ε4, the door to insulin-resistant dyslipidemia and brain fog? A case study. *Alzheimers Dement* (Amst). 2019;11:264-269. doi: 10.1016/j.dadm.2019.01.009.

15. Morrill SJ, Gibas KJ. Ketogenic diet rescues cognition in ApoE4+ patient with mild Alzheimer's disease: A case study. *Diabetes Metab Syndr.* 2019;13(2):1187-1191. doi: 10.1016/j.dsx.2019.01.035.

16. Evert AB, Dennison M, Gardner CD, et al. Nutrition Therapy for Adults with Diabetes or Prediabetes: A Consensus Report. *Diabetes Care.* 2019;42(5):731-754. doi: 10.2337/dci19-0014.

17. Lennerz BS, Barton A, Bernstein RK, et al. Management of Type 1 Diabetes with a Very Low-Carbohydrate Diet. *Pediatrics.* 2018;141(6):e20173349. doi: 10.1542/peds.2017-3349.

18. Sato K, Kashiwaya Y, Keon CA, Tsuchiya N, King MT, Radda GK, Chance B, Clarke K, Veech RL. Insulin, ketone bodies, and mitochondrial energy transduction. *FASEB J.* 1995;9(8):651-8. doi: 10.1096/fasebj.9.8.7768357.

19. Kashiwaya Y, King MT, Veech RL. Substrate signaling by insulin: a ketone bodies ratio mimics insulin action in heart. *Am J Cardiol.* 1997;80(3A):50A-64A. doi: 10.1016/s0002-9149(97)00458-x.

20. Kashiwaya Y, Takeshima T, Mori N, Nakashima K, Clarke K, Veech RL. D-beta-hydroxybutyrate protects neurons in models of Alzheimer's and Parkinson's disease. *Proc Natl Acad Sci U S A.* 2000;97(10):5440-4. doi: 10.1073/pnas.97.10.5440.

21. Costantini LC, Barr LJ, Vogel JL, Henderson ST. Hypometabolism as a therapeutic target in Alzheimer's disease. *BMC Neurosci.* 2008;9 Suppl 2(Suppl 2):S16. doi: 10.1186/1471-2202-9-S2-S16.

22. Veech RL, Chance B, Kashiwaya Y, Lardy HA, Cahill GF Jr. Ketone bodies, potential therapeutic uses. *IUBMB Life.* 2001;51(4):241-7. doi:10.1080/152165401753311780. PMID: 11569918.

23. Cahill GF Jr, Veech RL. Ketoacids? Good medicine? *Trans Am Clin Climatol Assoc.* 2003;114:149-61; discussion 162-3. https://pubmed.ncbi.nlm.nih.gov/12813917/

24. VanItallie TB, Nufert TH. Ketones: metabolism's ugly duckling. *Nutr Rev.* 2003;61(10):327-41. doi: 10.1301/nr.2003.oct.327-341.

25. Veech RL. The therapeutic implications of ketone bodies: the effects of ketone bodies in pathological conditions: ketosis, ketogenic diet, redox states, insulin resistance, and mitochondrial metabolism. *Prostaglandins Leukot Essent Fatty Acids.* 2004;70(3):309-19. doi: 10.1016/j.plefa.2003.09.007. PMID: 14769489.

26. Kashiwaya Y, Bergman C, Lee JH, et al. A ketone ester diet exhibits anxiolytic and cognition-sparing properties and lessens amyloid and tau pathologies in a mouse model of Alzheimer's disease. *Neurobiol Aging.* 2013;34(6):1530-9. doi: 10.1016/j.neurobiolaging.2012.11.023.

27. Wu Y, Gong Y, Luan Y, et al. BHBA treatment improves cognitive function by targeting pleiotropic mechanisms in transgenic mouse model of Alzheimer's disease. *FASEB J.* 2020;34(1):1412-1429. doi: 10.1096/fj.201901984R.

28. Yin JX, Maalouf M, Han P, et al. Ketones block amyloid entry and improve cognition in an Alzheimer's model. *Neurobiol Aging.* 2016;39:25-37. doi: 10.1016/j.neurobiolaging.2015.11.018.

29. Youm YH, Nguyen KY, Grant RW, et al. The ketone metabolite β-hydroxybutyrate blocks NLRP3 inflammasome-mediated inflammatory disease. *Nat Med.* 2015 Mar;21(3):263-9. doi: 10.1038/nm.3804.

30. Shippy DC, Wilhelm C, Viharkumar PA, Raife TJ, Ulland TK. β-Hydroxybutyrate inhibits inflammasome activation to attenuate Alzheimer's disease pathology. *J Neuroinflammation.* 2020;17(1):280. doi: 10.1186/s12974-020-01948-5.

31. Xiao YL, Gong Y, Qi YJ, Shao ZM, Jiang YZ. Effects of dietary intervention on human diseases: molecular mechanisms and therapeutic potential. *Signal Transduct Target Ther.* 2024;9(1):59. doi: 10.1038/s41392-024-01771-x.

32. Xu Y, Zheng F, Zhong Q, Zhu Y. Ketogenic diet as a promising non-drug intervention for Alzheimer's disease: Mechanisms and clinical implications. *J Alzheimers Dis.* 2023;92(4):1173-1198. doi: 10.3233/JAD-230002.

33. Rusek M, Pluta R, Ułamek-Kozioł M, Czuczwar SJ. Ketogenic diet in Alzheimer's disease. *Int J Mol Sci.* 2019;20(16):3892. doi: 10.3390/ijms20163892.

34. Castro CB, Dias CB, Hillebrandt H, et al. Medium-chain fatty acids for the prevention or treatment of Alzheimer's disease: a systematic review and meta-analysis. *Nutr Rev.* 2023;81(9):1144-1162. doi: 10.1093/nutrit/nuac104.

35. Sun L, Ye KX, Wong HLK, et al. The effects of medium chain triglyceride for Alzheimer's disease related cognitive impairment: A systematic review and meta-analysis. *J Alzheimers Dis.* 2023;94(2):441-456. doi: 10.3233/JAD-230406.

36. Price S, Ruppar TM. Ketogenic therapies in Parkinson's disease, Alzheimer's disease, and mild cognitive impairment: An integrative review. *Appl Nurs Res.* 2023;74:151745. doi: 10.1016/j.apnr.2023.151745.

37. Bohnen JLB, Albin RL, Bohnen NI. Ketogenic interventions in mild cognitive impairment, Alzheimer's disease, and Parkinson's disease: A systematic review and critical appraisal. *Front Neurol.* 2023 Feb 9;14:1123290. doi: 10.3389/fneur.2023.1123290.

38. Phillips MCL, Murtagh DKJ, Gilbertson LJ, Asztely FJS, Lynch CDP. Low-fat versus ketogenic diet in Parkinson's disease: A pilot randomized controlled trial. *Mov Disord. 2018* Aug;33(8):1306-1314. doi: 10.1002/mds.27390. Epub 2018 Aug 11.

39. Phillips MCL, Deprez LM, Mortimer GMN, et al. Randomized crossover trial of a modified ketogenic diet in Alzheimer's disease. *Alzheimers Res Ther.* 2021;13(1):51. doi: 10.1186/s13195-021-00783-x.

40. Castellano CA, Paquet N, Dionne IJ, et al. A 3-month aerobic training program improves brain energy metabolism in mild Alzheimer's disease: Preliminary results from a neuroimaging study. *J Alzheimers Dis.* 2017;56(4):1459-1468. doi: 10.3233/JAD-161163.

41. Abe S, Ezaki O, Suzuki M. Medium-chain triglycerides in combination with leucine and vitamin d benefit cognition in frail elderly adults: A randomized controlled trial. *J Nutr Sci Vitaminol (Tokyo).* 2017;63(2):133-140. doi: 10.3177/jnsv.63.133.

42. Abe S, Ezaki O, Suzuki M. Medium-chain triglycerides in combination with leucine and vitamin d increase muscle strength and function in frail elderly adults in a randomized controlled trial. *J Nutr.* 2016;146(5):1017-26. doi: 10.3945/jn.115.228965.

43. Abe S, Ezaki O, Suzuki M. Medium-chain triglycerides (8:0 and 10:0) increase Mini-Mental State Examination (MMSE) score in frail elderly adults in a randomized controlled trial. *J Nutr.* 2020 Sep 1;150(9):2383-2390. doi: 10.1093/jn/nxaa186.

44. Fortier M, Castellano CA, St-Pierre V, et al. A ketogenic drink improves cognition in mild cognitive impairment: Results of a 6-month RCT. *Alzheimers Dement.* 2021;17(3):543-552. doi: 10.1002/alz.12206.

45. Roy M, Rheault F, Croteau E, et al. Fascicle- and glucose-specific deterioration in white matter energy supply in Alzheimer's disease. *J Alzheimers Dis.* 2020;76(3):863-881. doi: 10.3233/JAD-200213.

46. Roy M, Edde M, Fortier M, et al. A ketogenic intervention improves dorsal attention network functional and structural connectivity in mild cognitive impairment. *Neurobiol Aging.* 2022;115:77-87. doi:10.1016/j.neurobiolaging.2022.04.005.

47. Myette-Côté É, St-Pierre V, Beaulieu S, et al. The effect of a 6-month ketogenic medium-chain triglyceride supplement on plasma cardiometabolic and inflammatory markers in mild cognitive impairment. *Prostaglandins Leukot Essent Fatty Acids.* 2021;169:102236. doi: 10.1016/j.plefa.2020.102236.

48. Fernando MG, Silva R, Fernando WMADB, et al. Effect of virgin coconut oil supplementation on cognition of individuals with mild-to-moderate Alzheimer's disease in Sri Lanka (VCO-AD Study): A randomized placebo-controlled trial. *J Alzheimers Dis.* 2023;96(3):1195-1206. doi: 10.3233/JAD-230670.

49. St-Pierre V, Vandenberghe C, Lowry CM, Fortier M, Castellano CA, Wagner R, Cunnane SC. Plasma Ketone and Medium Chain Fatty Acid Response in Humans Consuming Different Medium Chain Triglycerides During a Metabolic Study Day. Front Nutr. 2019 Apr 16;6:46. doi: 10.3389/fnut.2019.00046. PMID: 31058159; PMCID: PMC6481320.

50. Likhodii SS, Burnham WM. Ketogenic diet: does acetone stop seizures? *Med Sci Monit.* 2002;8(8):HY19-24. https://medscimonit.com/abstract/index/idArt/13550. PMID: 12165751.

51. Stonnington CM, Chen Y, Savage CR, et al. Predicting imminent progression to clinically significant memory decline using volumetric MRI and FDG PET. *J Alzheimers Dis.* 2018;63(2):603-615. doi: 10.3233/JAD-170852.

52. Reiman EM, Chen K, Alexander GE, et al. Functional brain abnormalities in young adults at genetic risk for late-onset Alzheimer's dementia. *Proc Natl Acad Sci U S A.* 2004;101(1):284-9. doi: 10.1073/pnas.2635903100.

53. de la Monte SM, Wands JR. Review of insulin and insulin-like growth factor expression, signaling, and malfunction in the central nervous system: relevance to Alzheimer's disease. *J Alzheimers Dis.* 2005;7(1):45-61. doi: 10.3233/jad-2005-7106.

54. de la Monte SM, Wands JR. Alzheimer's disease is type 3 diabetes-evidence reviewed. *J Diabetes Sci Technol.* 2008;2(6):1101-13. doi: 10.1177/193229680800200619.

55. Simpson IA, Chundu KR, Davies-Hill T, Honer WG, Davies P. Decreased concentrations of GLUT1 and GLUT3 glucose transporters in the brains of patients with Alzheimer's disease. *Ann Neurol.* 1994;35(5):546-51. doi: 10.1002/ana.410350507.

56. Jia D, Wang F, Yu H. Systemic alterations of tricarboxylic acid cycle enzymes in Alzheimer's disease. *Front Neurosci.* 2023;17:1206688. doi: 10.3389/fnins.2023.1206688.

57. Castellano CA, Nugent S, Paquet N, et al. Lower brain 18F-fluorodeoxyglucose uptake but normal 11C-acetoacetate metabolism in mild Alzheimer's disease dementia. *J Alzheimers Dis.* 2015;43(4):1343-53. doi: 10.3233/JAD-141074.

58. Newport MT, VanItallie TB, Kashiwaya Y, King MT, Veech RL. A new way to produce hyperketonemia: use of ketone ester in a case

of Alzheimer's disease. *Alzheimers Dement.* 2015;11(1):99-103. doi: 10.1016/j.jalz.2014.01.006.

59. USDA FoodData Central (usda.gov) https://fdc.nal.usda.gov/

60. Kivipelto M, Mangialasche F, Ngandu T. Lifestyle interventions to prevent cognitive impairment, dementia, and Alzheimer disease. *Nat Rev Neurol.* 2018;14(11):653-666 . doi: 10.1038/s41582-018-0070-3.

61. Norwitz NG, Jaramillo JG, Clarke K, Soto A. Ketotherapeutics for neurodegenerative diseases. *Int Rev Neurobiol.* 2020;155:141-168. doi: 10.1016/bs.irn.2020.02.003.

62. Mattson MP, Moehl K, Ghena N, Schmaedick M, Cheng A. Intermittent metabolic switching, neuroplasticity, and brain health. *Nat Rev Neurosci.* 2018;19(2):63-80. doi: 10.1038/nrn.2017.156.

63. Watanabe S and Tsujino S. Applications of Medium-Chain Triglycerides in Foods. *Front. Nutr.* 2022;9:802805. doi: 10.3389/fnut .2022.802805

64. Blackburn GL, Babayan VK. Infant feeding formulas using coconut oil and the medium chain triglycerides. *J Am Coll Nutr.* 1989;8(3): 253-4. doi: 10.1080/07315724.1989.10720300.

65. Hamosh M, Bitman J, Wood L, Hamosh P, Mehta NR. Lipids in milk and the first steps in their digestion. *Pediatrics.* 1985;75(1 Pt 2):146-50. PMID: 3880885.

66. Gutiérrez-García AG, Contreras CM, Díaz-Marte C. Myristic acid in amniotic fluid produces appetitive responses in human newborns. *Early Hum Dev.* 2017;115:32-37. doi: 10.1016/j.earlhumdev.2017.08.009.

67. Cunnane SC, Menard CR, Likhodii SS, Brenna JT, Crawford MA. Carbon recycling into de novo lipogenesis is a major pathway in neonatal metabolism of linoleate and alpha-linolenate. *Prostaglandins Leukot Essent Fatty Acids.* 1999;60(5-6):387-92. doi: 10.1016/s09 52-3278(99)80018-0.

68. Augustin K, Khabbush A, Williams S, Eaton S, Orford M, Cross JH, Heales SJR, Walker MC, Williams RSB. Mechanisms of action for the medium-chain triglyceride ketogenic diet in neurological and metabolic disorders. *Lancet Neurol.* 2018;17(1):84-93. doi: 10.1016/S1474-4422(17)30408-8.

69. Andersen JV, Westi EW, Neal ES, Aldana BI, Borges K. β-Hydroxybutyrate and medium-chain fatty acids are metabolized by different cell types in mouse cerebral cortex slices. *Neurochem Res.* 2023;48(1):54-61. doi: 10.1007/s11064-022-03726-6.

70. Nonaka Y, Takagi T, Inai M, Nishimura S, Urashima S, Honda K, Aoyama T, Terada S. Lauric acid stimulates ketone body production in the KT-5 astrocyte cell line. *J Oleo Sci.* 2016;65(8):693-9. doi: 10.5650/jos.ess16069.

71. Itzhaki RF, Lathe R, Balin BJ, et al. Microbes and Alzheimer's Disease. *J Alzheimers Dis. 2016*;51(4):979-84. doi: 10.3233/JAD-160152.

72. Goc A, Niedzwiecki A, Rath M. In vitro evaluation of antibacterial activity of phytochemicals and micronutrients against Borrelia burgdorferi and Borrelia garinii. *J Appl Microbiol.* 2015;119(6):1561-72. doi: 10.1111/jam.12970.

73. Kabara JJ, Swieczkowski DM, Conley AJ, Truant JP. Fatty acids and derivatives as antimicrobial agents. Antimicrob Agents Chemother. 1972 Jul;2(1):23-8. doi: 10.1128/ AAC.2.1.23. PMID: 4670656; PMCID: PMC444260.

74. Thormar H, Isaacs CE, Brown HR, Barshatzky MR, Pessolano T. Inactivation of

enveloped viruses and killing of cells by fatty acids and monoglycerides. *Antimicrob Agents Chemother.* 1987;31(1):27-31. doi: 10.1128/AAC.31.1.27.

75. Dayrit, F.M. The properties of lauric acid and their significance in coconut oil. *J Am Oil Chem Soc* 2015; **92**:1-15 (2015). https://doi.org/10.1007/s11746-014-2562-7 .

76. Dodge JA, Sagher FA. Antiviral and antibacterial lipids in human milk and infant formula. *Arch Dis Child.* 1991;66(2):272-3. doi: 10.1136/adc.66.2.272-b.

77. Currenti W, Godos J, Alanazi AM, Lanza G, Ferri R, Caraci F, Grosso G, Galvano F, Castellano S. Dietary fats and cognitive status in Italian middle-old adults. *Nutrients.* 2023;15(6):1429. doi:10.3390/nu15061429.

78. Mett J, Lauer AA, Janitschke D, et al. Medium-Chain Length Fatty Acids Enhance Aβ Degradation by Affecting Insulin-Degrading Enzyme. *Cells.* 2021;10(11):2941. doi: 10.3390/cells10112941.

79. Nishimura Y, Moriyama M, Kawabe K, Satoh H, Takano K, Azuma YT, Nakamura Y. Lauric acid alleviates neuroinflammatory responses by activated microglia: Involvement of the GPR40-dependent pathway. *Neurochem Res.* 2018;43(9):1723-1735. doi: 10.1007/s11064-018-2587-7.

80. Shaheryar ZA, Khan MA, Hameed H, Mushtaq MN, Muhammad S, Shazly GA, Irfan A, Jardan YAB. Natural fatty acid guards against brain endothelial cell death and microvascular pathology following ischemic insult in the presence of acute hyperglycemia. *Biomedicines.* 2023;11(12):3342. doi:10.3390/biomedicines11123342.

81. Chatterjee P, Fernando M, Fernando B, et al. Potential of coconut oil and medium chain triglycerides in the prevention and treatment of Alzheimer's disease. *Mech Ageing Dev.* 2020;186:111209. doi: 10.1016/j.mad.2020.111209.

82. Illam SP, Narayanankutty A, Raghavamenon AC. Polyphenols of virgin coconut oil prevent pro-oxidant mediated cell death. *Toxicol Mech Methods.* 2017;27(6):442-450. doi: 10.1080/15376516.2017.1320458.

83. Nafar F, Clarke JP, Mearow KM. Coconut oil protects cortical neurons from amyloid beta toxicity by enhancing signaling of cell survival pathways. *Neurochem Int.* 2017;105:64-79. doi: 10.1016/j.neuint.2017.01.008.

84. Nafar F, Mearow KM. Coconut oil attenuates the effects of amyloid-β on cortical neurons in vitro. *J Alzheimers Dis.* 2014;39(2):233-7. doi: 10.3233/JAD-131436.

85. Neelakantan N, Seah JYH, van Dam RM. The effect of coconut oil consumption on cardiovascular risk factors: A systematic review and meta-analysis of clinical trials. *Circulation.* 2020;141(10):803-814. doi: 10.1161/CIRCULATIONAHA.119.043052.

86. Assunção ML, Ferreira HS, dos Santos AF, Cabral CR Jr, Florêncio TM. Effects of dietary coconut oil on the biochemical and anthropometric profiles of women presenting abdominal obesity. *Lipids.* 2009;44:593–601. doi:10.1007/s11745-009-3306-6

87. Vijayakumar M, Vasudevan DM, Sundaram KR, Krishnan S, Vaidyanathan K, Nandakumar S, Chandrasekhar R, Mathew N. A randomized study of coconut oil versus sunflower oil on cardiovascular risk factors in patients with stable coronary heart disease. *Indian Heart J.* 2016;68:498–506. doi:10.1016/j.ihj.2015.10.384

88. Korrapati D, Jeyakumar SM, Putcha UK, Mendu VR, Ponday LR, Acharya V, Koppala

SR, Vajreswari A. Coconut oil consumption improves fat-free mass, plasma HDL-cholesterol and insulin sensitivity in healthy men with normal BMI compared to peanut oil. *Clin Nutr.* 2019;38:2889– 2899. doi:10.1016/j.clnu.2018.12.026.

89. Reiser R, Probstfield JL, Silvers A, Scott LW, Shorney ML, Wood RD, O'Brien BC, Gotto AM Jr, Insull W Jr. Plasma lipid and lipoprotein response of humans to beef fat, coconut oil and safflower oil. *Am J Clin Nutr.* 1985;42:190–197. doi:10.1093/ajcn/42.2.190

90. Mendis S, Kumarasunderam R. The effect of daily consumption of coconut fat and soya-bean fat on plasma lipids and lipoproteins of young normolipidaemic men. *Br J Nutr.* 1990;63:547–552. doi:10.1079/bjn19900141

91. Heber D, Ashley JM, Solares ME, Wang HJ, Alfin-Slater RB. The effects of a palm-oil enriched diet on plasma lipids and lipoproteins in healthy young men. *Nutr Res.* 1992;12:S53-S59. doi:10.1016/S0271-5317(05)80450-6.

92. McKenney JM, Proctor JD, Wright JT Jr, Kolinski RJ, Elswick RK Jr, Coaker JS. The effect of supplemental dietary fat on plasma cholesterol levels in lovastatin-treated hypercholesterolemic patients. *Pharmacotherapy.* 1995;15:565–572. doi:10.1002/j.1875-9114.1995.tb02864.

93. Lu Z, Hendrich S, Shen N, White PJ, Cook LR. Low linolenate and commercial soybean oils diminish serum HDL cholesterol in young free-living adult females. *J Am Coll Nutr.* 1997;16:562–569. PMID: 9430084.

94. Voon PT, Ng TK, Lee VK, Nesaretnam K. Diets high in palmitic acid (16:0), lauric and myristic acids (12:0 + 14:0), or oleic acid (18:1) do not alter postprandial or fasting plasma homocysteine and inflammatory markers in healthy Malaysian adults. *Am J Clin Nutr.* 2011;94:1451-1457. doi:10.3945/ajcn.111.020107.

95. Harris M, Hutchins A, Fryda L. The impact of virgin coconut oil and higholeic safflower oil on body composition, lipids, and inflammatory markers in postmenopausal women. *J Med Food.* 2017;20:345–351. doi: 10.1089/jmf.2016.0114

96. Khaw KT, Sharp SJ, Finikarides L, Afzal I, Lentjes M, Luben R, Forouhi NG. Randomised trial of coconut oil, olive oil or butter on blood lipids and other cardiovascular risk factors in healthy men and women. *BMJ Open.* 2018;8: e020167. doi:10.1136/bmjopen-2017-020167

97. Oliveira-de-Lira L, Santos EMC, de Souza RF, Matos RJB, Silva MCD, Oliveira LDS, Nascimento TGD, Schemly P, Souza SL. Supplementationdependent effects of vegetable oils with varying fatty acid compositions on anthropometric and biochemical parameters in obese women. *Nutrients.* 2018;20:E932. doi:10.3390/nu10070932.

98. Maki KC, Hasse W, Dicklin MR, Bell M, Buggia MA, Cassens ME, Eren F. Corn oil lowers plasma cholesterol compared with coconut oil in adults with above-desirable levels of cholesterol in a randomized crossover trial. *J Nutr.* 2018;148:1556–1563. doi:10.1093/jn/nxy156

99. McKenzie KM, Lee CM, Mijatovic J, Haghighi MM, Skilton MR. Medium-chain triglyceride oil and blood lipids: A systematic review and meta-analysis of randomized trials. *J Nutr.* 2021;151(10):2949-2956. doi: 10.1093/jn/nxab220.