Summary

Diet suggestions:

1 walnut each meal: antioxidant and anti-inflammatory, and metal chelator

ALA(446mg/whole Walnut) (meets recommended sup amount) for TNF inhibitor and conversion into EPA and DHA(protection from calcium dysregulation) Omega 3's VITAMIN E (γ-TOCOPHEROL) (1mg/whole Walnut) RDI 15mg/day

Polyphenols: (125mg/whole Walnut) RDI 500-1500mg/day

2 Brazil Nuts/day: for selenium, take with probiotic meal, and possibly with pterostilbene

reduce sugar and saturated fats (artificial sweeteners likely OK, but avoid aspartame)

omega-6: 3 fatty acids adequate ratio (5:1) Omega 3 best types EPA DHA, Best obtained from foods especially Salmon

Carotenoids, antioxidant vitamin C, and vitamin B6, lutein/zeaxanthin, (consume with fat or cooked whole egg) (hard to get recommended RDI from diet, might need supplements)

Potassium (Potassium Chloride, Potassium Gluconate, Potassium Aspartate, Potassium Citrate)

Source: leafy vegs, legumes, salmon(384mg), banana(358mg), potatoes(russet in skin)(550mg) RDA: 4700mg/d (<2% of adults meet this goal) FDA has limit set on 99mg so hard to supplemental

Potatoes boil them whole or bake, roast, or microwave them (don't peel them)

Use "Salt Substitutes" 800mg/1/4 tsp "Nu-Salt"

-note: people with kidney disease, may have problems with Potassium (this is controversial lately)

Cruciferous fruits in Diet: Food Sources: Broccoli(raw), Brussels Sprouts, Cabbage, Cauliflower, Kale, Watercress, Turnips, Radish (-or Sulforaphane Supplement Broccole Sprout extract) Noringa oleifera leaf powder: use with cooking(smooties, muffins, quick bread, steeped as a tea or sprinkled into soups and salad dressings), or use as Supplement

Add Spices to meals: Cloves, cinnamon(ceylon), black pepper, rosemary(on Potatoes), garlic, red peppers(capsaicin), Sesame seed, parsley, saffron, curcumin, ginger, star anise, ginseng

Polyphenols (goal >500-1500mg/day)

Sources: Olive Oil(use for cooking), Dark Chocolate(3448mg/100g), Blueberries(560-836mg/100g), Strawberries(235mg), apple(136mb), Nuts(hazelnut495mg), walnuts(28mg), almonds(187mg), pecans(493mg), red Onion(168mg), Cloves(15188mg/100g), Dried Peppermint(11960mg/100g), star Anise(5460mg/100g), Cocoa Powder(3448mg/100g), Dried Sage and Rosemary,

Ferulic acid (FA), Polyphenol, (hydroxycinnamic acid) Sources: Popcorn(313mg), cooked sweetcorn(42mg), bamboo(243mg), whole grain rye bread(54mg), oatmeal(25-52mg),

rice, citrus fruits Recommended 150-250mg/day (take with Curcumin for added effect)

avoid foods with Aluminum Phosphate as food additive for leavening agent (cake mixes)

Supplement suggestions:

Chamomile -Apigenin (anti-oxidant), improves sleep : drink chamomile tea with dried parsley) Amazon Twinings of London Herbal Camomile Tea Bags \$0.25/bag

lutein/zeaxanthin if not enough in diet (Amazon: Webber \$0.30/softgel)

Taurine (Amino Acid, regulates calcium) Amazon Taurine Powder \$0.15/serving of 2.5g (mix in juice drink)

Caprylic Acid (C8) (to generate ketones for brain) 1ml(2.5g) in coffee 3x/day (Amazon \$0.05/ml)

Liposomal Glutathione Anti-oxidant, anti-inflammarcy, liver detoxm heavy metal chelator Recommended Supplement: 50-600mg/day (Amazon \$0.67/250mg dose) 5-HTP in increase Serotonin Levels (regulation of sleep, depression, anxiety, aggression, appetite) (caution if used with other serotonin boosting drugs) (Amazon \$0.16/100mg *3 day)

Ashawagandha herb(Withaferin A?) for AD, Supplement: >300mg twice/day? (Amazon \$0.60/day)

Bacopa monnieri Herb for AD, Supplement: 300-400 mg per day (Amazon \$0.50/500mg)

Black Seed Oil (herbal ingredient, polyphenols and antioxidants) 1-2 teaspoons/day (ensure TQ quantity is high) (Amazon \$0.75/tsp)

Gotu Kola (Centella asiatica) anti-oxidant, improve mood, TNF alpha inhibitor, Amazon 475mg (\$0.09/count) (twice/day?)

Slibinin - Milk Thistle (combine with curcumin) Supplement: 300-900mg/day (Amazon \$0.09/250mg *3day)

Saffon - neuroprotective, 15mg twice per day (\$0.63/15mg)

Broccole Sprout Extract 1000mg (to get 70mg of Sulforaphane) (Amazon \$0.37/1000mg)

Moringa oleifera (Amazon \$0.10/1g 1-2 times daily)

Polyphenols (many types act differently)

Anthocyanin (antioxidants+TNF inhibitor): >100mg/day average, eat in fruits like blueberries (likely no need to supplement if eating right fruits daily)

(optional Cranberry&Elderberry Concentrate 5ml/day) 120ml \$22 (\$1/day) Immunia has other selections too.

Carnosine (anti-oxidate, copper -chelating, neuroprotectic) only from meats, recommend supplement: 250 mg of carnosine per day (Amazon \$0.50/500mg)

Curcumin (anti-inflammatory, antioxidant, metal chelator)-use bioavailable form such as Longvida 500-2000mg/day (or take more of the piperine type) combine with Slibinin/Ferulic Acid Amazon Turmeric Curcumin with Piperine 1500mg.(actually only 300mg) \$0.15/count *2/day

Grape Seed Extract (iron chelator, anti-inflammator) Supplement dosage: 25-300mg/day (Amazon \$0.22/100mg *2/day) pterostilbene 100mg twice/day, inhibits amyloid-β-induced neuroinflammation for AD, good for gut microbiome (Amazon \$0.47/100mg *2/day) Quercetin -anti-oxidant, TNF inhibitor Supplement Levels: Typ 500-1000mg/day (take with Vitamin C to enhance bioavailability?) Maybe LipoMicel brand (Amazon \$0.52/250mg 1-3 times/day)

Vitamins as supplements

Vitamin A : eat plenty of fruits and vegetables that are rich in carotenoids (best not to supplement) Vitamin B: B2, B3, B6, B9(folic acid), B12

Choline(Vitamin B4) RDI: 550mg/day Sources: Salmon 1 filet: 242 mg (44% DV), Eggs 1 large egg: 147 mg (27% DV) Recommend Supplement if not enough in diet.

Vitamin C

Vitamin D: (possible caution) VITAMIN E (y-TOCOPHEROL) : 15mg/day

Vitamin K is not well-absorbed through supplementation; the best way to add it to your diet is through vegetables high in Vitamin K

MicroNutrients:

Avoid Aluminum food additives, Arsenic, Cadmium, Mercury Need. Boron supplement 3 mg/day Chromium RDA: 30mcg Male, 20mcg Female (supplement could benefit) Copper (requires right level- homeostatis) Iron (yes but need iron chelator) Lithium (maybe under doctor) Magnesium RDI 320mg female, 420mg male, maybe supplement Manganese (both low and high levels bad)(just accept what you get in food like nuts) Selenium (Brazil Nuts) Silicon(green beans, bananas) Vandadium (ground parsley, black pepper) Zinc?

Body/Brain Shortage with AD:

GABA levels glutathione (GSH) low glutathione peroxidase (GPX) activity serum levels of lycopene and lutein+zeaxanthin choline ?? Selenium zinc lower serum levels of DHA (Omega 3) potassium and rubidium levels . serotonin maybe Manganese (Mn) decreased brain glucose uptake are linked to AD-glucose in the brain is much lower than that in the blood of AD patients potassium and rubidium levels low levels of vitamin B-12 and the risk of AD lower levels of folic acid vitamin D deficiency some types of gut bacteria Past Taurine Intake https://pubmed.ncbi.nlm.nih.gov/28849444/

Excess in AD patients:

Brain: Alum, Calcium, iron copper, Arsenic, Mercury linked a low intake of PUFAs and a high intake of cholesterol and SFAs Sugar excess tumor necrosis factor-alpha (TNF-alpha) urinary arsenic blood chromium some types of gut bacteria

Markers: (blood, Cerebral Spinal Fluid CSF, PET, MRI)

linked to the formation of brain "plaques" and "tangles" made of excess proteins called beta amyloid: amyloid beta (AB) i (accumulation of amyloid-beta protein (AB)) TNF alpha APOE4 gene

inflammation, CRP

cerebrospinal fluid (CSF) levels of total Tau (T-tau), phosphorylated Tau (P-Tau) and beta-amyloid peptide (AB42)

Risk Factors, co-morbities:

older age (HR, 8.06; 95% CI, 6.69-9.72 for participants aged 60-66 years) https://pubmed.ncbi.nlm.nih.gov/28783817/ lower educational attainment (HR, 1.61; 95% CI, 1.28-2.03 for less than a high school education) <u>https://pubmed.ncbi.nlm.nih.gov/28783817/</u> APOE ε4 genotype (HR, 1.98; 95% CI, 1.78-2.21) <u>https://pubmed.ncbi.nlm.nih.gov/28783817/</u> midlife smoking (HR, 1.41; 95% CI, 1.23-1.61) https://pubmed.ncbi.nlm.nih.gov/28783817/ diabetes (HR, 1.77; 95% Cl, 1.53-2.04) https://pubmed.ncbi.nlm.nih.gov/28783817/ type 2 diabetes 1.34. https://pubmed.ncbi.nlm.nih.gov/35272707/ mid life high blood pressure, (statin drugs reduce risk) hypertension (HR, 1.39; 95% Cl, 1.22-1.59) https://pubmed.ncbi.nlm.nih.gov/28783817/ midlife hypertension and late-life hypotension group (HR, 1.62 [95% Cl, 1.11-2.37]) https://pubmed.ncbi.nlm.nih.gov/31408138 obesitv Tinnitus 1.5. .https://pubmed.ncbi.nlm.nih.gov/32699252/ Stroke 1.59. https://pubmed.ncbi.nlm.nih.gov/25096624/ heart disease

Arthritis (RA) [unless taking anti-TNF agent:etanercept], psoriasis and psoriatic arthritis. 1.88 https://pubmed.ncbi.nlm.nih.gov/33192461/ Resting heart rate: RHR≥80 (vs. 60-69) bpm was associated with a multi-adjusted hazard ratio of 1.55 https://pubmed.ncbi.nlm.nih.gov/34859936/ Microvascular Ischemic Disease (blockage to small blood vessels in brain) https://www.md-health.com/Chronic-Microvascular-Ischemic-Disease.html

Theories on Causes:

Genetics Calcium Heavy Metals: 'aluminum hypothesis', mercury (dental amalgam (which contains about 50% mercury) Gut MicroBiome (use of anti-bodies) Nutrition/Diet: (certainity a factor) Vascular Disturbances: diminished Blood flow Glucose level in Brain Chemical Factors: interference with neurotransmitters or chemical messengers (1) acceleration of aging,

(2) degeneration of anatomical pathways, including the cholinergic and cortico-cortical pathways,

(3 environmental factors such as exposure to aluminium, head injury, and malnutrition,

(4) genetic factors including mutations of amyloid precursor protein (APP) and presenilin (PSEN) genes, and allelic variation in apolipoprotein E (Apo E),

(5) a metabolic disorder resulting from mitochondrial dysfunction,

(6) vascular factors such as a compromised blood brain barrier,

(7) <u>immune system</u> dysfunction, and inflammation (8) infectious agents.

Main Theory: The amyloid hypothesis (goal is to make sure that amyloid plaques do not appear.)(plaques - clumps of amyloid-beta protein)

Aß cascade hypothesis (Aß peptides have long been viewed as a potential target for AD which dominated new drug research during the past twenty years)

Tau hypothesis Neurofibrillary tangles, another intracellular hallmark of AD, are composed of tau

Inflammation hypothesis Reactive gliosis and neuroinflammation are hallmarks of AD. Microglia-related pathways were considered to be central to AD risk and pathogenesis, as supported by emerging genetic and transcriptomic studies

Cholinergic and oxidative stress hypothesis Acetylcholine (ACh) is an important neurotransmitter used by cholinergic neurons, which has been involved in critical physiological processes, such as attention, learning, memory, stress response, wakefulness and sleep, and sensory information [59-63]. Cholinergic neurons damage was considered to be a critical pathological change that correlated with cognitive impairment in AD.

Glucose hypometabolism Glucose hypometabolism is the early pathogenic event in the prodromal phase of AD, and associated with cognitive and functional decline. Early therapeutic intervention before the irreversible degeneration has become a consensus in AD treatment.

Methods of treatment:



Ferulic Acid https://pubmed.ncbi.nlm.nih.gov/34963433/

Gotu Kola https://pubmed.ncbi.nlm.nih.gov/32079355/

Huperzia (huperzine A) https://pubmed.ncbi.nlm.nih.gov/26745980/

Ptychopetalum olacoides https://pubmed.ncbi.nlm.nih.gov/12895682/ Saffron https://pubmed.ncbi.nlm.nih.gov/22655699/

Sage https://pubmed.ncbi.nlm.nih.gov/24413832/

Rosemay/Rosmaric Acid https://www.tandfonline.com/doi/full/10.3109/14756366.2015.1135914 Shankhpushpi, https://pubmed.ncbi.nlm.nih.gov/35212831/

TNF alpha Inhibitors:

https://pubmed.ncbi.nlm.nih.gov/27470609/ Treatment for Rheumatoid Arthritis and Risk of Alzheimer's Disease: A Nested Case-Control Analysis 2016

AD was more prevalent (p < 0.0001) among RA patients (0.79 %) than among those without RA (0.11 %). Exposure to anti-TNF agents as a class, but not other

immunosuppressive drugs studied, was associated with lowered risk of AD among RA patients (unadjusted OR 0.44; 95 % CI 0.22-0.87; p = 0.02; adjusted OR 0.45; 95 % CI 0.23-0.90; p = 0.02). Sub-group analysis demonstrated that of the three anti-TNF agents studied, only etanercept (unadjusted OR, 0.33; 95 % CI 0.08-0.94; p = 0.03; adjusted OR 0.30; 95 % CI 0.08-0.89; p = 0.02) was associated with a decreased risk of AD in RA patients.

Conclusion: There is an increased risk of AD in the studied RA population. The relative risk of AD among RA subjects was lowered in those exposed to etanercept. Anti-TNF therapy with etanercept shows promise as a potential treatment for AD.

https://pubmed.ncbi.nlm.nih.gov/18220520/ Perispinal etanercept for treatment of Alzheimer's disease. 2007

Results: Continued open-label clinical experience with this new treatment modality, now for more than two years, suggests that weekly maintenance treatment with perispinal etanercept may have a sustained positive effect. In addition, rapid clinical improvement, within minutes of dosing, has been observed on a repeated basis in multiple patients.

alpha lipoic acid https://pubmed.ncbi.nlm.nih.gov/11689467/

Ashwagandha https://pubmed.ncbi.nlm.nih.gov/26667305/

Black Seed Oil Thymoquinone https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4549173/

Coenzyme Q10 https://pubmed.ncbi.nlm.nih.gov/20354351/

Curcumin https://pubmed.ncbi.nlm.nih.gov/23425071/

Green Tea / EGCG https://pubmed.ncbi.nlm.nih.gov/17135765/

Magnesium https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5988891/

Milk Thistle https://pubmed.ncbi.nlm.nih.gov/10586080/

Tart Cherry Juice https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7961347/pdf/molecules-26-01403.pdf

Vitamin E / Alpha Tocopheral https://pubmed.ncbi.nlm.nih.gov/30471562/

Prevention:

https://www.alzdiscovery.org/cognitive-vitality/first-steps

- 1. Ėat for your Brain
- 2. Get Enough Sleep
- 3. Exercise 4. Alleviate Stress
- 5. Be Social
- 6. Keep Learning
- 7. Manage Chronic Illness

Supplements

https://www.sciencedirect.com/science/article/abs/pii/S0014299921001278?via%3Dihub

Specifically, numerous NPs including flavonoids, gingerols, tannins, anthocyanins, triterpenes and alkaloids have been shown anti-inflammatory, antioxidant, anti-amyloidogenic, and anti-cholinesterase properties.