Alzheimer’s Disease is the Most Common Type of Dementia.

- Dementia is a general term describing degenerative brain disorders characterized by loss of short term memory, confusion and disorientation.

- Alzheimer’s disease accounts for about 65% of dementia cases with the rest being due to Lewy Body Dementia, vascular dementia, Frontotemporal dementia and other disorders.

- Diagnosis requires a neurologic exam, neuropsychometric testing, brain imaging and blood tests to eliminate deficiencies of B12, thyroid hormone (and vitamin D).

- Available treatments are not sufficient.
Invasive and Noninvasive Routes To Overcome the Blood-brain Barrier.

Intranasal Delivery to the Brain.

- Is non-invasive.
- Bypasses the blood-brain barrier.
- Results in rapid extracellular delivery to the brain and spinal cord along both the olfactory and trigeminal pathways involving perineural and perivascular channels.
- Reduces or eliminates systemic exposure.
- Does not require modification of the therapeutic agent.
- Works best for potent therapeutics.

Robert Thorne first demonstrated the trigeminal pathway for drug delivery to the CNS.
Iron accumulates abnormally in the brain in virtually all neurodegenerative disorders including: Alzheimer’s, Parkinson’s, stroke, hemorrhage, Traumatic Brain Injury, Huntington’s Disease and ALS.

Iron is a potent promoter of oxidative and free radical damage which inactivates the human brain receptor required for memory and other key brain components required for movement and function.

• Deferoxamine (DFO) is a generic drug that binds iron with exceptionally high affinity $10^{31}$, that has been used to treat iron overload in the blood in humans for decades.

• Intramuscular DFO has been shown in a two year clinical trial in patients with Alzheimer’s to reduce cognitive decline by 50% but has significant side effects, and does not cross the blood-brain barrier well.

• Consequently, we have developed and patented intranasal DFO to treat Alzheimer’s, Parkinson’s, Stroke, and Traumatic Brain Injury.

Intranasal DFO Protects Dopamine Cells and Improves Memory & Movement.

- I.N. DFO protects dopamine nerve cells and improves movement in animals with Parkinson’s disease in both the genetic and the neurotoxin models of Parkinson’s.

- Just a few nose drops of DFO given before or after a stroke, reduces brain damage in rats by 55%.


- When funding is available, this treatment can be tested in humans with Alzheimer’s, Parkinson’s, stroke and TBI.

Alzheimer’s Patients’ Brains Do Not Take Up Glucose Properly.

Glucose Uptake & Utilization (FDG-PET)

Alzheimer’s Patient

Normal Elderly Adult

Insulin Signaling Deficiency in the Brains of Alzheimer’s Patients.

• Both the amount of insulin (insulin gene expression) and insulin signaling are reduced in the brains of Alzheimer’s patients causing a metabolic disorder “type 3 diabetes” or “diabetes of the brain” which leaves brain cells starved for energy and unable to function normally.

• Insulin resistance characterizes the insulin signaling deficit in Alzheimer’s brain.
Intranasal Insulin for Alzheimer’s Disease.

• The issuing of my 1989 and 1999 patent filings claiming direct intranasal delivery of insulin to the brain to treat Alzheimer’s disease and Parkinson’s disease have been followed by a number of human clinical trials by ourselves and others.

• Five trials in Alzheimer’s patients and five trials in normal human adults demonstrated improved memory following intranasal insulin treatment with no change in the blood levels of insulin or glucose.
Intranasal Insulin Improves Memory in Patients with Alzheimer’s Disease.

• A single intranasal insulin treatment acutely improved verbal memory for adults with Alzheimer’s disease within 15 minutes at doses that did not alter blood levels of insulin or glucose.¹

• Intranasal insulin (20 IU bid) for 21 days enhanced delayed recall (memory) compared to placebo (p = .03) and significantly improved attention (p = .01) and functional status (p = .04).

• However, it is possible that only the long-acting intranasal insulin detemir will improve memory in Alzheimer’s patients who carry the APOE-4 gene allele. This could be 35% or more of patients with the disease.
Longer Trials of Intranasal Insulin in AD.

• Intranasal insulin (10 or 20 iu bid) improved memory, cognition and function in patients (N ≈ 30) in the early stages of AD or with MCI in a four month clinical trial.

• It also reduced the loss of glucose uptake and utilization as measured by FDG PET imaging in key brain regions.

• Additional trials are needed to obtain FDA approval, and the NIH has now provided 7.9 million dollars to conduct those trials at other research centers.

• The longest trial of intranasal insulin, funded by donors, is being conducted at our Center for Memory & Aging in St. Paul. We are using both a newer nasal spray device and newer form of insulin.

• We are also testing this treatment in older adults with Down Syndrome.
Can Intranasal Insulin Improve the Brain Pathology of Alzheimer’s Disease?

• Insulin can provide energy needed to prevent brain degeneration and replace worn out parts of brain cells.

• Insulin increases Insulin Degrading Enzyme, the enzyme that degrades beta amyloid, and reduces GSK3beta that phosphorylates tau to form Alzheimer’s tangles.

• Insulin maintains synaptic density.

• If humans are given intranasal insulin at the first sign of a deficiency of insulin in the brain, it may be able to delay or prevent the onset and progression of the disease.
Diabetes Doubles the Risk for Alzheimer’s Disease.

- Diabetes doubles the risk for getting Alzheimer’s disease which is not surprising since diabetics have a deficiency of insulin signaling.
- Intranasal insulin prevents cognitive decline and brain atrophy in aging diabetic animals.
- Human studies are needed to determine if intranasal insulin can reduce the risk of Alzheimer’s disease in the millions of people with diabetes.
- Intranasal insulin improves cognition in individuals with Type 2 diabetes and may be beneficial in those with Type 1 as well.
Intranasal Adult Stem Cells Treat Brain Disorders in Animals.

- Intranasal adult stem cells bypass the blood-brain barrier and specifically target the damaged areas of the brain in animals.
- Intranasal stem cells are anti-inflammatory and can produce the therapeutic proteins needed by the brain to promote repair and treat neurodegenerative disorders.
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<td>Ninomiya et al. (2015)</td>
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Preventing Memory Loss and Reducing the Risk for Alzheimer’s Disease.

• Exercise

• Diet

• Socialization

• Maintaining high normal blood levels of vitamin D

• Maintaining normal blood levels of vitamin B12

• Maintaining normal blood levels of thyroid hormone.
Plants and Humans Evolved Together.

• Plants are not only the major source of food and nutrients in our diet required for health but also are the source of many of our medicines.

• Plants are the original source for perhaps 40% of the pharmaceuticals in use in the United States today.

• Foods derived from plants can have both nutrient and pharmacologic effects on our brains.
The Mediterranean Diet.

The principal aspects of this diet include proportionally high consumption of olive oil, legumes, unrefined cereals, fruits, and vegetables, moderate to high consumption of fish, moderate consumption of dairy products (mostly as cheese and yogurt), moderate wine consumption, and low consumption of non-fish meat and non-fish meat products.
The Mediterranean Diet is Associated with Less Brain Atrophy!

- A cross-sectional study of 647 elderly adults without dementia based on a food frequency questionnaire and MRI measures of brain volumes.

- Mediterranean Diet adherence was associated with less brain atrophy, with an effect similar to 5 years of aging. Higher fish and lower meat intake might be the two key food elements that contribute to the benefits of this diet on brain structure.

Mediterranean diet (MeDi) and brain structure in a multiethnic elderly cohort, Gu et al. from Columbia University, Neurology 2015;85:1-8.
The Mediterranean Diet is Associated with Larger Brain Volume!

• Compared to lower Mediterranean Diet adherence, higher adherence was associated with larger brain volume, gray matter volume and white matter volume.

• Higher fish and lower meat intakes were associated with larger gray matter volume. Lower meat intake was also associated with larger brain volume.

• Higher fish intake was associated with larger mean cortical thickness. Volumes of hippocampus (memory area) and other brain areas were associated with the dietary factors.
Mediterranean Diet Components Are Good for the Brain.

• Fish contains Vitamin D, polyunsaturated fatty acids (omega-3 and omega-6 fatty acids and DHA), and B vitamins.

• Authors note that Vitamin D protects against beta amyloid deposition and inflammation. Low Vitamin D has been linked to brain atrophy and increased Alzheimer’s disease.

• Authors state that B vitamins play a role in slowing brain atrophy. (B3, B6, B12 may slow cognitive decline in MCI.)

• Authors indicate that diets high in meat can promote Alzheimer’s disease including insulin resistance, amyloid generation and tau phosphorylation.
The MIND Diet Is Associated with Reduced Incidence of Alzheimer’s Disease.

These authors investigated the diet-Alzheimer’s disease relationship in a prospective study of 923 participants, ages 58 to 98 years, followed on average 4.5 years. Diet was assessed by a semi-quantitative food frequency questionnaire.

MIND diet associated with reduced incidence of Alzheimer’s disease, Bennett and Aggarwal from Rush University and Harvard School of Public Health, Alzheimer’s & Dementia 2015;11(9):1007-14.
Greater Adherence to MIND Diet Inversely Correlates to Incidence of Alzheimer’s Disease.

- This prospective study of the MIND diet score provides evidence that greater adherence to the overall dietary pattern may be protective against the development of Alzheimer’s.

- The estimated effect was a 53% reduction in the rate of Alzheimer’s disease for persons in the highest tertile of MIND scores and a 35% reduction for the middle tertile of scores compared with the lowest tertile.
MIND Diet versus Mediterranean Diet.

• In contrast to the MIND diet, only the highest adherence to the Mediterranean diet was associated with Alzheimer’s disease prevention.

• These data suggest that even modest adherence to the MIND diet score may have substantial benefits for the prevention of AD.
Benefits of the MIND Diet.

• Results of the study suggest that even modest adjustments to diet may help to reduce one’s risk of developing AD. For example, the MIND diet score specifies just two vegetable servings per day, two berry servings per week, and one fish meal per week.

• Based on this study, high quality diets such as the Mediterranean diet can be modified, such as in the MIND diet, to provide better protection against dementia.
Details of the MIND Diet.

These 10 food groups are included:

• Green leafy vegetables (spinach, kale, chard, collard greens and salad greens): At least six servings a week
• Other vegetables: At least one a day
• Nuts: Five servings a week (walnuts, pistachios, sunflower nuts)
• Berries: (blueberries, strawberries) Two or more servings a week
• Beans: At least three servings a week
• Whole grains: Three or more servings a day
• Fish: Once a week (salmon, tuna, herring, sardines, black cod)
• Poultry (chicken or turkey): Two times a week
• Olive oil: Use it as your main cooking oil.
• Wine: One glass a day
Food groups to avoid:
• Red meat: Less than four servings a week
• Butter and margarine: Less than a tablespoon daily
• Cheese: Less than one serving a week
• Pastries and sweets: Less than five servings a week
• Fried or fast food: Less than one serving a week
Fish/Seafood Consumption and AD.

- Moderate seafood consumption (≥ 1 meal[s]/week) was correlated with less Alzheimer disease neuropathology. Although seafood consumption was also correlated with higher brain levels of mercury, these levels were not correlated with brain neuropathology.

M.C. Morris et al. AMA. 2016;315(5):489-497.
Better white matter integrity in humans is associated with consuming a diet rich in foods containing omega fatty acids and vitamin E, i.e. fish, nuts, cereals, and vegetables.

The strength of the association was about the same magnitude as a 10-year increase in age, which is a well-established factor contributing to white matter integrity deterioration.

White matter integrity is associated with cognitive function, and it mediates the relationship between this nutrient rich diet pattern and cognitive function.

J. A. Luchsinger et al. ANN NEUROL 2016;79:1014–1025
Anti-inflammatory components of food could lead to the development of therapeutics that could help to reduce the risk of AD or perhaps even assist in its treatment.

These include flavonoids such as **Quercetin** that is found in numerous foods including: canned capers, raw red onions, raw white onions, citrus fruits, cherries, blueberries, cranberries, raw black plums, ancho peppers, green chile peppers, red leaf lettuce, raw kale, cooked asparagus, buckwheat, red wine, tea and coco powder.

Quercetin Ameliorates Alzheimer’s Pathology and Improves Cognition in a Mouse Model.

- Quercetin decreased beta amyloid, tauopathy, astrogliosis and microgliosis in the brain.
- Quercetin improved performance on learning and spatial memory tasks.
- Quercetin reverses the pathology of Alzheimer’s disease and protects cognitive and emotional function in this aged triple transgenic mouse model of Alzheimer’s disease.


• Free brain iron, elevated in Alzheimer’s disease and other brain disorders, generates free radicals that inactivate the memory receptor.

• Iron removal from cells is enhanced by deferoxamine.

• Quercetin penetrates cell membranes via glucose transport proteins and chelates intracellular iron.

• Quercetin, a component of food, could also be used to bind and transport iron out of brain cells to treat Alzheimer’s.

Quercetin and Deferoxamine Both Prevent Brain Cell Loss in a Rat Model of Parkinson’s.

- The iron chelators quercetin and deferoxamine both prevent dopaminergic neuronal loss in rat model of Parkinson’s.
- Quercetin and deferoxamine both maintain dopamine levels in the 6-OHDA model of Parkinson’s.
- The combination of quercetin and deferoxamine treatments is more effective than either treatment alone.

Quercetin Protects Against Cell Death and Enhances Cognition in Rat Models of Parkinson’s.

- In the 6-OHDA model of Parkinson’s disease, quercetin enhances spatial memory.
- In the rotenone model of Parkinson’s, quercetin protects against programmed cell death of dopaminergic neurons.

Cognitive-Enhancing Effect of Quercetin in a Rat Model of Parkinson's Disease Induced by 6-Hydroxydopamine. Evidence-Based Complementary and Alternative Medicine 2012 Article ID 823206.

Conclusions About Brain Healthy Diets.

- Studies suggest that the MIND diet and the Mediterranean diet reduce the risk of developing Alzheimer’s disease.

- Components of these diets, including vitamin D, B-vitamins, omega fatty acids and bioflavonoids such as quercetin likely contribute to these benefits.

- Turmeric, cinnamon, green tea, etc. are also likely helpful.

- Diet, exercise and remaining socially and mentally active are important for maintaining brain health and preventing Alzheimer’s and other brain disorders.

Call 800-229-2872 for information or to donate.
Following the MIND Diet:
It’s tough, but someone has to do it.
Intranasal Treatment References.


Diet References.


• Mediterranean Dietary Pattern and Depression: The PREDIMED Randomized Trial. Almudena Sánchez-Villegas et al. in BMC Medicine, Vol. 11, Article No. 208; September 20, 2013.

• Early Intervention to Preempt Major Depression among Older Black and White Adults. Charles F. Reynolds et al. in Psychiatric Services, Vol. 65, No. 6, pages 765–773; June 2014.
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• MIND diet associated with reduced incidence of Alzheimer’s disease, Bennett and Aggarwal from Rush University and Harvard School of Public Health, Alzheimer’s & Dementia 2015;11(9):1007-14.

• White Matter Integrity as a Mediator in the Relationship between Dietary Nutrients and Cognition in the Elderly J. A. Luchsinger et al. ANN NEUROL 2016;79:1014–1025

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Call us at 651-254-7000
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Press 2: To Make a Donation or for Research Information