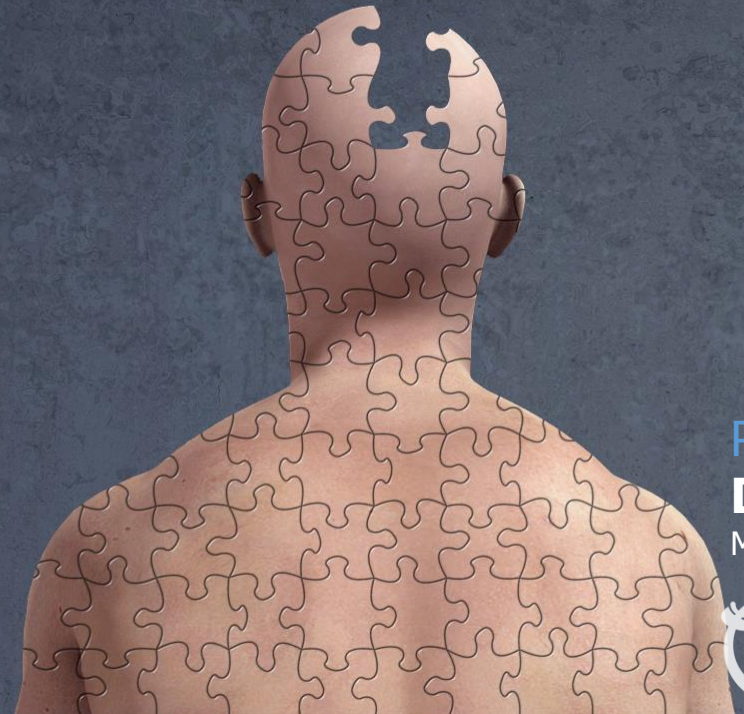
Awakening from Alzheimer's

Can we Help Reverse Cognitive Decline?



Presented by:

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Member Institute for Functional Medicine

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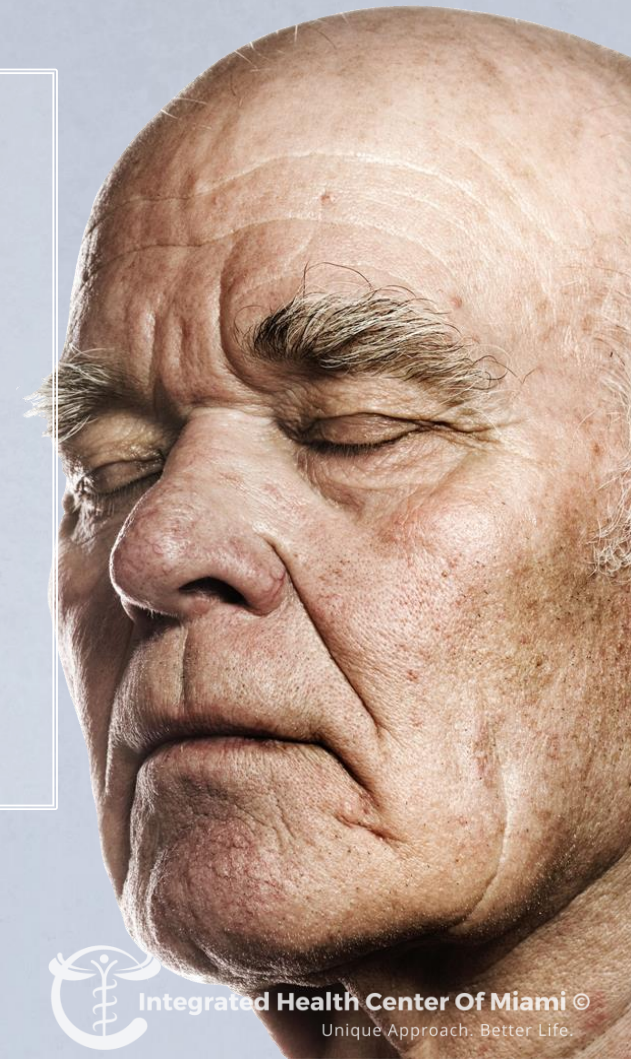
Topics

01. Prevalence & Impact
02. Current Model
03. Emerging Model
04. Classification System
05. Testing and Treatment

Every

:06

<u>Seconds</u> someone is diagnosed with Alzheimer's Disease.



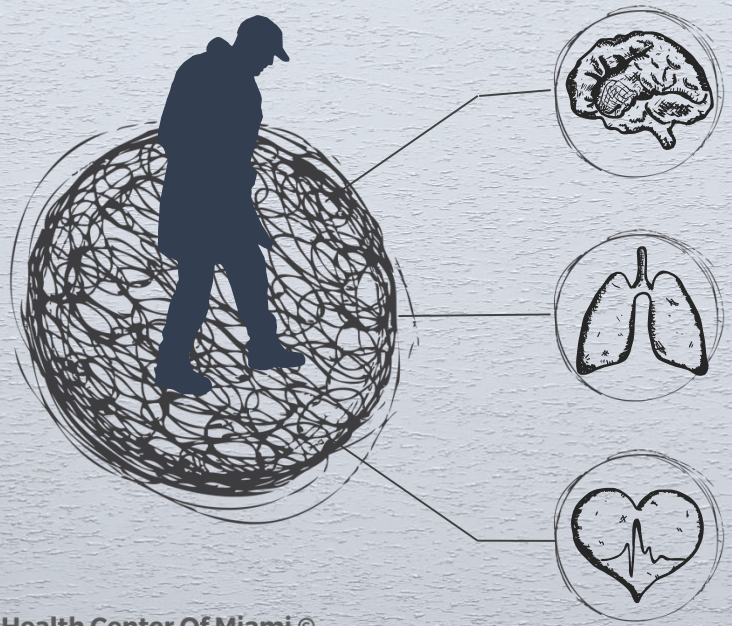
Important Stats

- **Cognitive decline** is a major concern of the aging population, and Alzheimer's disease is the major cause of age-related cognitive decline, with approximately **5.4 million American patients and 30 million affected globally[1].**

In the **absence of effective prevention and treatment**, the prospects for the future are of great concern, with 13 million Americans and 160 million globally projected for 2050, leading to **potential bankruptcy of the Medicare system**.

The Cruelest Disease

Alzheimer's disease and it's complications robs the patient of everything that is held dear in the ilife from treasured memories, higher functions, family members and eventually life itself.



Severe Brain Degeneration

Volumetric Imaging has revealed that Alzheimers disease tends to start with shrinkage of the hippocampus, eventually spreading to the whole brain and affecting all higher functions.
Eventually showing the hallmarks of the disease which are Amyloid Plaques and Tau Fragments.

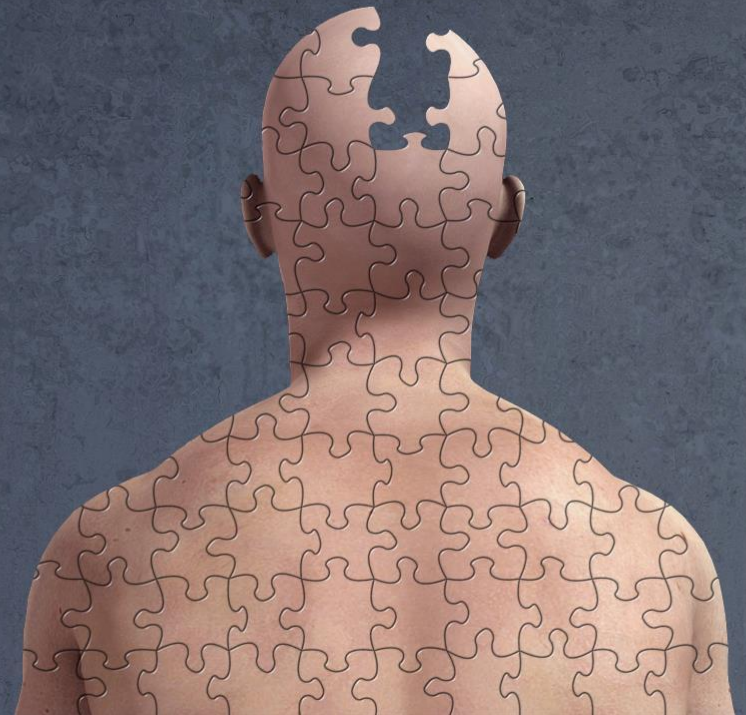
Respiratory Complications

Most Late Stage Alzheimers patients pass away from a cruel and painful death in the form of Aspiration Pneumonia due to the loss of essential body functions like swallowing.

Heart Break

Loss of memory often results in the need from separation from the family nucleus which will often result in neglect, depression, suffering
and life being cut short.

Diagnosis and Current Management of Alzheimer's Disease



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MCI, Dementia and Alzheimer's

Three of the new guidelines focus on three stages of Alzheimer's disease:

(1) Dementia due to Alzheimer's,
(2) Mild cognitive impairment (MCI) due to Alzheimer's, and
(3) Preclinical (pre-symptomatic) Alzheimer's.

* The fourth guideline updates criteria for documenting and reporting Alzheimer's-related changes observed during an autopsy.

http://www.alz.org/research/diagnostic_criteria/

Preclinical Stage

1.The guidelines on preclinical Alzheimer's define this condition as a newly recognized stage of the disease. In **a "preclinical" disease stage, key biological changes Are under way in the body, but the disease has not yet caused any noticeable "clinical" symptoms.**

2. Current scientific evidence suggests that in preclinical Alzheimer's, brain changes caused by the disease may begin years — or even decades — before symptoms such as memory loss and confusion occur.

3.The guidelines are not an immediate call for diagnosis of this preclinical stage and do not include specific diagnostic criteria.

4. They rather propose a research agenda to identify biomarkers that may signal When these presymptomatic brain changes begin.

http://www.alz.org/research/diagnostic_criteria/

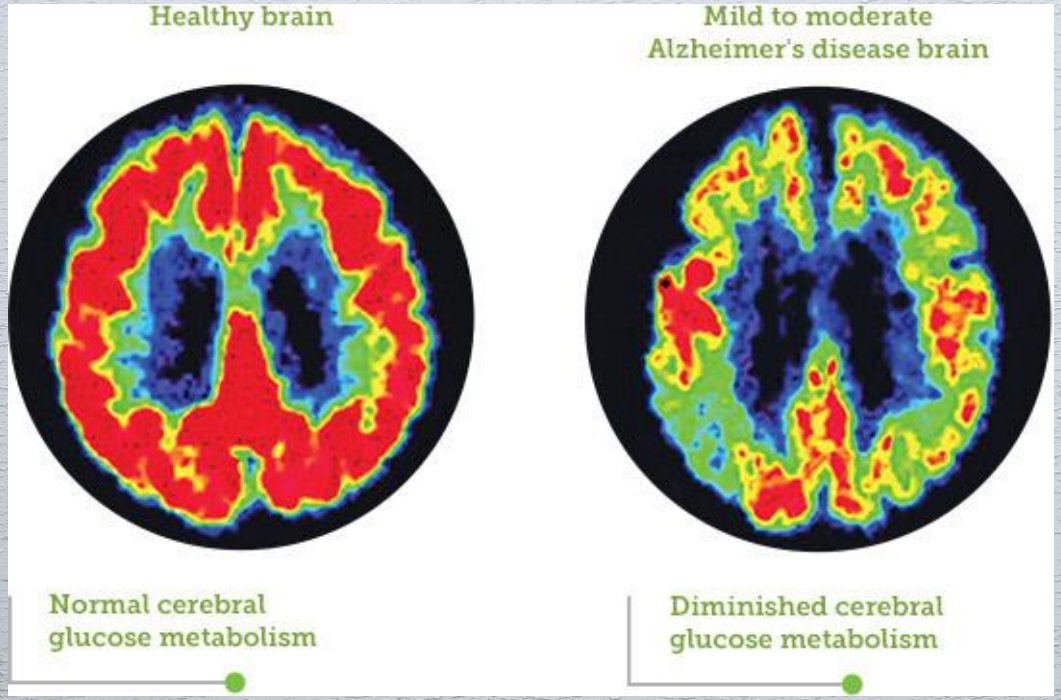
Biomarkers for AD Dx

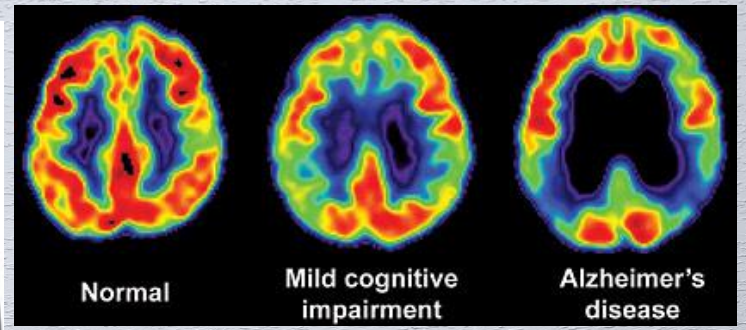
The strongest biomarker candidates for Alzheimer's disease include brain imaging studies using magnetic resonance imaging (MRI) or positron emission tomography (PET), and proteins in cerebrospinal fluid (CSF).

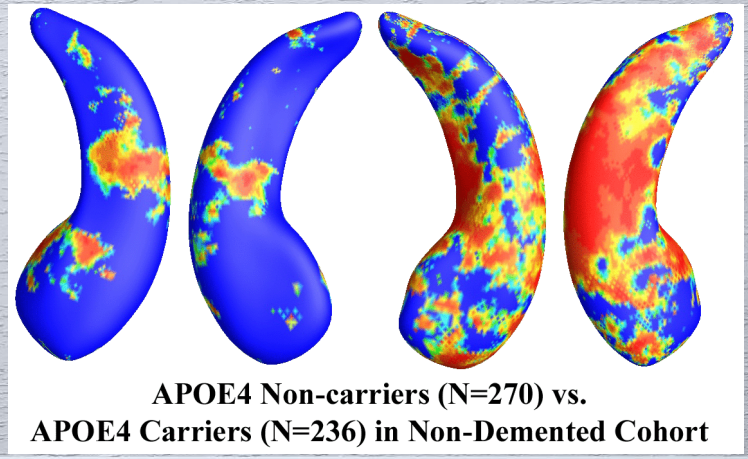
Identification of the newly defined preclinical stage of Alzheimer's will gain importance if researchers succeed in developing treatments that can slow or stop the progression of Alzheimer's. Such treatments **may be most effective** if used as early as possible in the course of the illness.

http://www.alz.org/research/diagnostic_criteria/

Brain Imaging







APOE4 Non-carriers (N=270) vs.
APOE4 Carriers (N=236) in Non-Demented Cohort

CSF Markers of AD

A combination of more than one biomarker in CSF, such as CSF p-tau, t-tau, and A*β42 is considered to give higher diagnostic accuracy of AD. It can identify AD, prodromal AD, and also can differentiate AD from other dementia with high sensitivity and specificity that is otherwise impossible to achieve.*

Although CSF biomarkers have proved to be highly informative, sensitive, and specific for detection of clinical AD and early stage of AD, their regular use in clinic is still limited. One of the major reasons against the vast applicability of CSF in AD diagnosis is lumbar puncture, an invasive method to collect the CSF sample. Other issues including inconsistency of data analysis of CSF sample due to sample collection, transportation, storage, and high expense of the test might limit the use of CSF for routine diagnosis.

Int J Alzheimer Dis. 2010; 2010: 606802.

Functional Usefulness..

In a Functional Medicine model these are not a priority since we are working to understand and address the drivers behind the neurodegeneration.

Let the neurologist worry about the disease, we will worry about the driving Forces and root causes.

STAGING YOU MUST KNOW

Preclinical Alzheimer's Disease

Stage 1

This is a newly defined stage of the disease reflecting current evidence that measureable biomarker changes in the brain may occur years before symptoms affecting memory, thinking or behavior can be detected by affected individuals or their physicians. While the guidelines identify these preclinical changes as an Alzheimer's stage, they do not establish diagnostic criteria that doctors can use now. Rather, th ey propose additional research to establish which biomarkers may best confirm that Alzheimer's-related changes are underway and how best to measure them.

Free-access paper: Reisa A. Sperling et al. "Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging – Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease." *Alzheimer's & Dementia: The Journal of the Alzheimer's Association 2011;7(3):280 – 292.Workgroup members: Proposed criteria for preclinical Alzheimer's disease*

RED FLAGS OF NEURODEGENERATION

1. Mental Fog (Earliest Symptoms)
1. Mental Fatigue
1. Decreased Sharpness and or Recall Speed
1. Forgetfulness
1. Difficulty Recalling Recent events (Converting short into long ter m memory)
1. Depression (Very Strong Clinical indicator of Neurodegeneration).

Mild Cognitive Decline (MCI) due to AD

Stage 2

In this stage, mild changes in memory and thinking are noticeable and can be measured on mental status tests, but are not severe enough to disrupt a person's day-to-day life. This guideline details four levels of certainty for ruling out other causes of MCI and arriving at a diagnosis of MCI due to Alzheimer's. Only the first level of certainty, which relies on core clinical criteria similar to those used today, is currently recommended for widespread use in general clinical practice. More research is needed before the other three levels of uncertainty, which incorporate biomarkers, may be useful outside research settings.

Free-access paper: Marilyn S. Albert et al. "The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging – Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease." *Alzheimer's & Dementia: The Journal of the Alzheimer's Association 2011;7(3):270 – 279.*

Mental Status Exam

See Attachment. You need to be good at this.

Dementia due to Alzheimer's Disease:

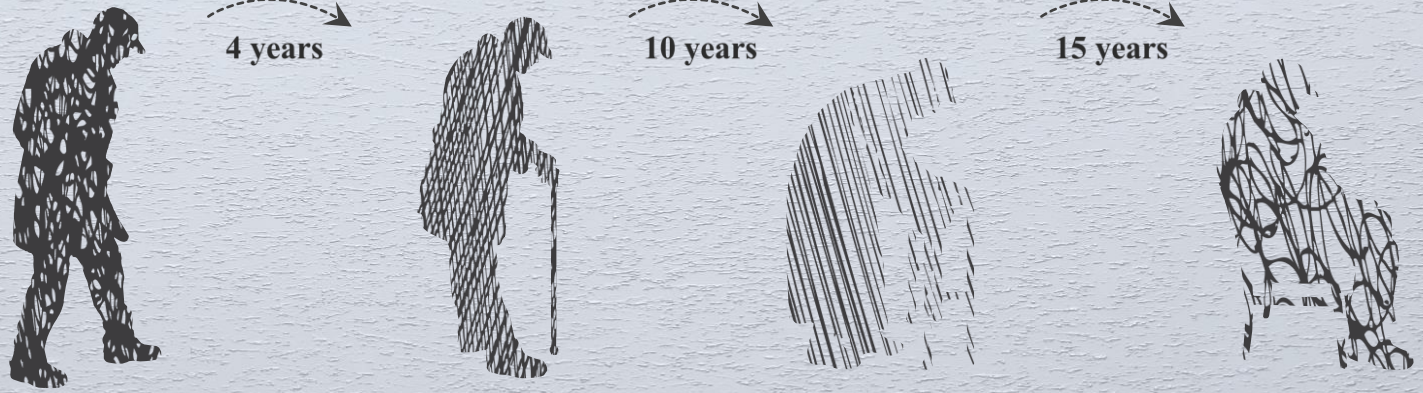
Stage 3 and on…

In this stage, impairments in memory, thinking and behavior decrease a person's ability to function independently in everyday life. This guideline updates and clarifies clinical criteria to diagnose dementia from all causes and specifically from Alzheimer's disease. These criteria are sufficiently broad and flexible to be used now both by community practitioners without access to neuropsychological testing, specialized brain imaging, or CSF testing and by specialists engaged in research or clinical studies who have access to such tools. In the future, biomarker evidence may provide additional diagnostic certainty, but much more research is needed to identify the most accurate biomarkers and confirm their usefulness. **Staging 1-4 and End Stage**

Free-access paper: Guy M. McKhann et al. "The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging – Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease." *Alzheimer's & Dementia: The Journal of the Alzheimer's Association 2011;7(3):263 – 269.*

Stages of Alzheimer's Disease

.Alzheimer's Dementia has 7 Identifiable stages. Preclinical and MCI are left out of the graphic. Additionally the times between each stage are just estimates as the disease will manifest differently in each patient based on the underlying mechanism of disease.



Stage 3

Mild Decline

1. finding the right word during conversations
2. remembering names of new acquaintances
3. planning and organizing

Stage 4

Moderate Decline

1. Have difficulty with simple arithmetic
2. May forget details about their life histories
3. Have poor short term memory (may not recall what they ate for breakfast, for example)
4. Inability to manage finance and pay bills

Stage 5

Moderately Severe Decline

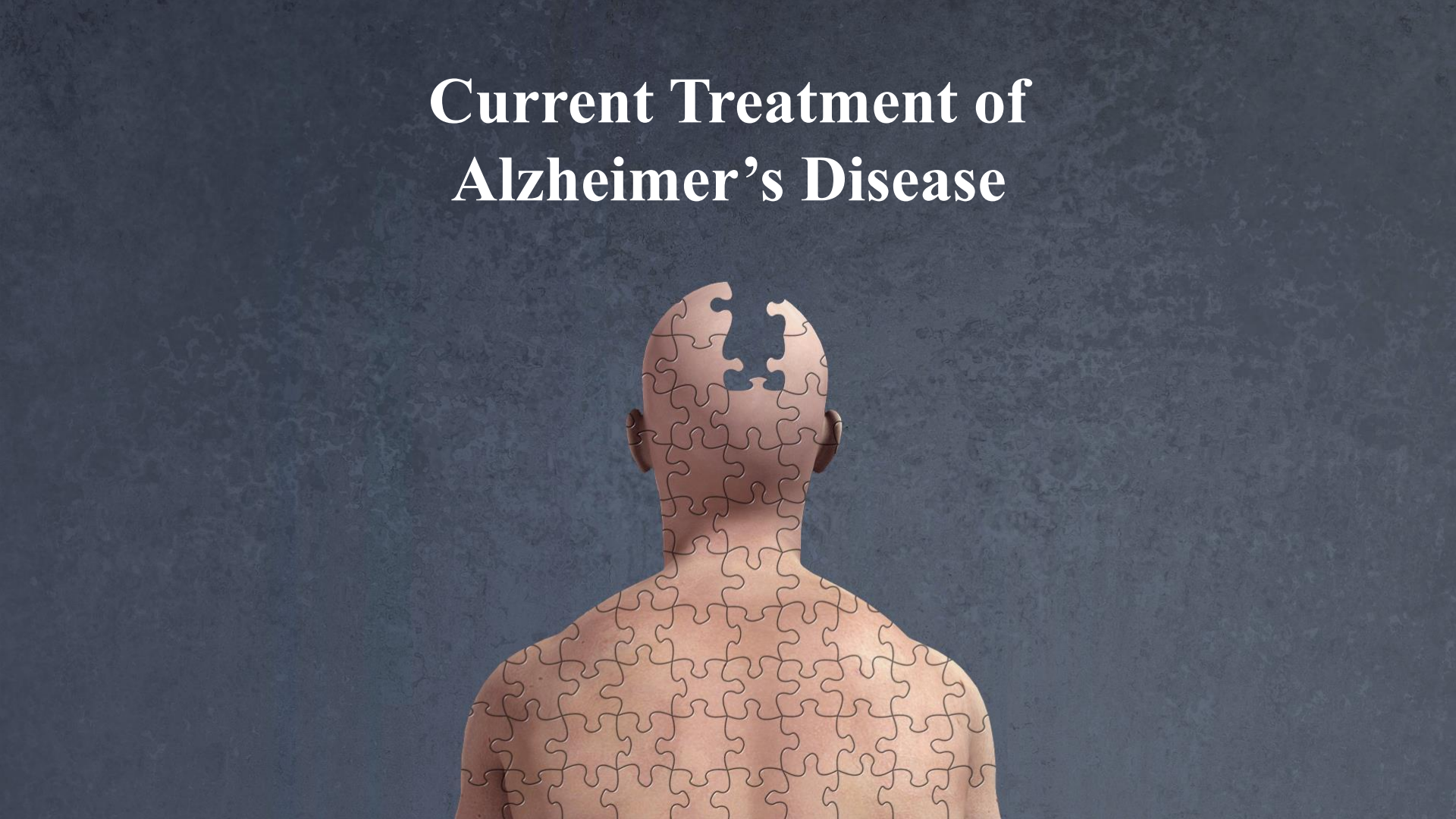
1. Significant confusion
2. Inability to recall simple details about themselves such as their own phone number
3. Difficulty dressing appropriately (Can still bathe and use toilet)

Stage 6 & 7

Severe Decline and Very Severe Decline

Assisted Living and Professional Care. Nearing Death and Death.

Current Treatment of Alzheimer's Disease



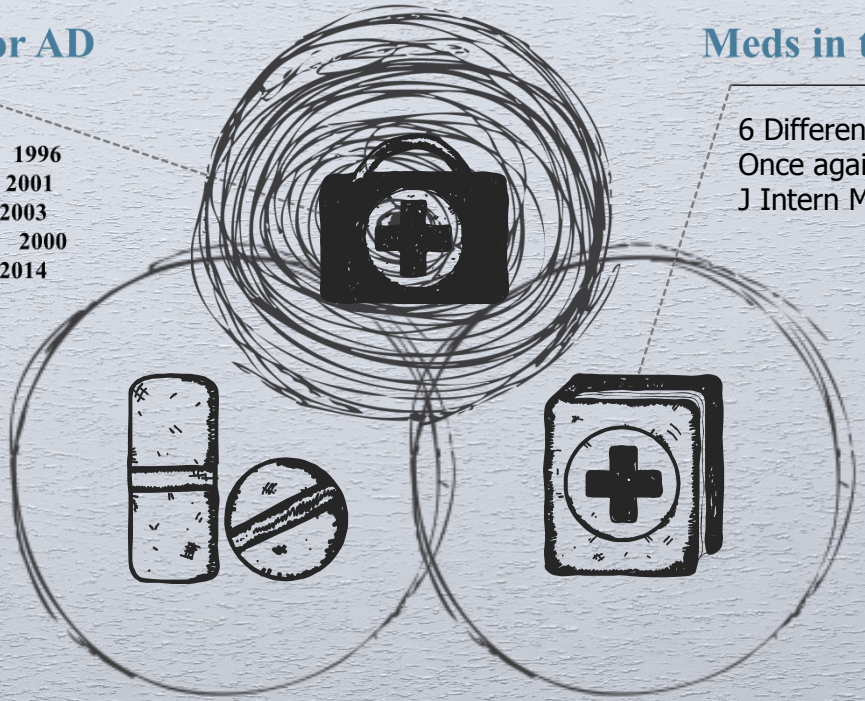
The Greatest Failure of Modern Medicine

The lack of progress despite substantial effort may rest, as stated by Leber, a former FDA director, 'Not in our methods, but in our ignorance' [129]. (Clinical trials and late-stage drug development for Alzheimer's disease: an appraisal from 1984 to 2014). I AGREE BUT SUPER DISAGREE.

Currently Approved Meds for AD

FDA Approved			
1. donepezil	Aricept	All stages	1996
2. galantamine	Razadyne	Mild to moderate	2001
3. memantine	Namenda	Moderate to severe	2003
4. rivastigmine	Exelon	All stages	2000
5. Donepezil	Namzaric	Moderate to severe	2014

At best these might relief the worse symptoms for a very brief period of time



Meds in the Pipeline for MCI

6 Different Clinical Trials underway.
Once again not great promise at all.
J Intern Med March 01 2015

Important Note on Causation vs. Correlation.

1.Many patients got worse and reached endstage alzheimer's with the newest category of drug which is Anti-amyloid.

2.WHY?

Failed Rat Study, Stupidly Followed by failed human study with 2600 subjects (Eli Lilly)

https://www.statnews.com/2015/11/09/top-alzheimers-approach-makes-mice-brains-worse/

http://www.forbes.com/sites/robertlangreth/2010/08/17/eli-lilly-alzheimers-failure-bolsters-skeptics-on-amyloid-theory/#11e081af38e9

Current Medical Perspective

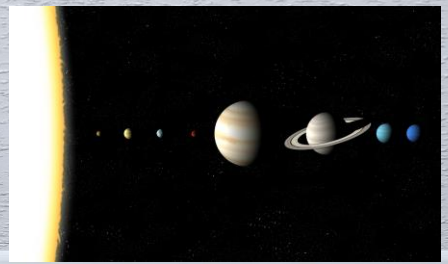
PMC full text:
J Am Med Dir Assoc. Author manuscript; available in PMC 2016 Sep 1.
Published in final edited form as:
J Am Med Dir Assoc. 2015 Sep 1; 16(9): 731–739.
doi: 10.1016/j.jamda.2015.06.017

Table 4
Recommendations for the Management of Early Cognitive Impairment
Spend enough time with the patient and, when appropriate, family members, to ensure maximum understanding of the condition and recommended care.
Provide written instructions. When necessary, engage a care partner to help carry out recommendations.
Identify all potentially reversible causes of cognitive impairment.
Provide advice regarding lifestyle practices and follow-up on implementation:
- The Mediterranean or similar diet including olive oil
- Physical exercise
- Intellectual activities
- CST for persons with early or moderate AD

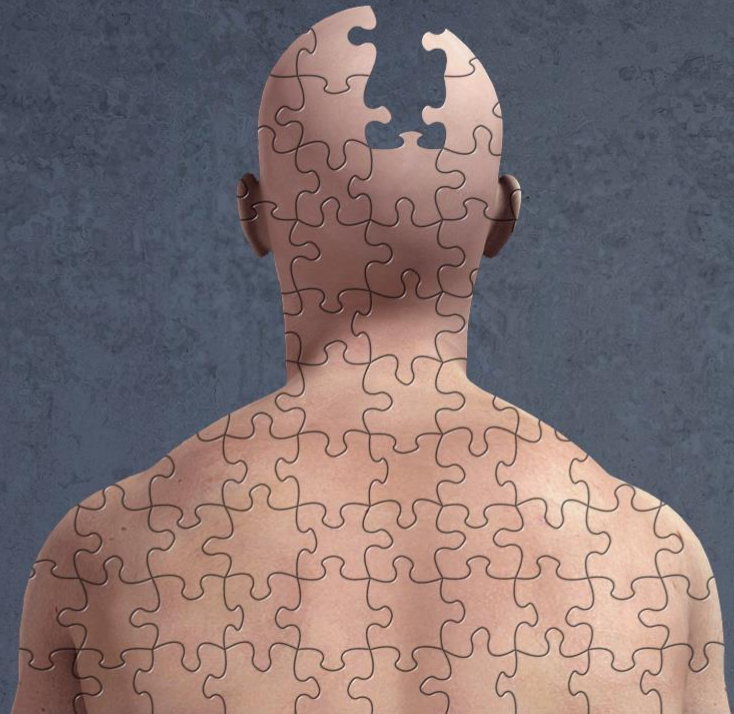
Discuss the potential use of cholinesterase inhibitors in persons with AD
Encourage the person to develop advanced directives for health, legal, and financial matters, and follow-up on whether this was done
Educate the patient and family through recognized specialty organizations (eg, the Alzheimer's Association in the US)
Address, and take steps to avoid, major risks associated with cognitive impairment (eg, money management, "safe return" bracelet, appropriate disposition of unsafe tools and guns, driving)
Encourage identification and use of support services (eg, support groups, family and friend engagement activities)
Talk about potential research participation and help the person to make his or her own informed decisions

Why I Think we are perfectly positioned.

1. The Interventions that have shown promise are the things we are most highly trained at. Many of them we are already doing clinically as FM practitioners.
2. In the event that we cannot help an individual patient he/she will be no worse than they would with any form of conventional management, which will absolutely guarantee the progression of their disease. If anything it is my sincere perspective and educated belief that they are better off with us in their corner. YOU ARE A BAD ASS.
3. It is urgent that we create a united voice for the rescuing of the brains of the millions that are now afflicted and the hundreds of millions that will be afflicted.
4. If it was your own brain, what would you do?

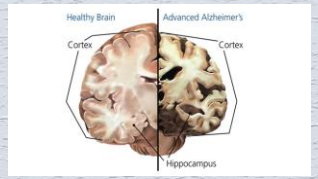


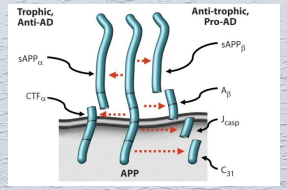
So what the hell is really going on?



The Progression of Root Cause

Why treating at the top does not work.





3.

2.

1.

1. Metabolic Push

Ongoing Inflammation
Trophic Defficiencies
Toxic Illness
Glycotoxicity
Genetics

2. Prionic Loop

Abnormal Cleaving of APP resulting in prionic fragments that result in neurite retraction overpowering neurite extension, commonly also signaling caspase mediated apoptosis.

3. Hallmarks of AD

Advanced deposition of AB, Hippocampal Atrophy, TAU fragments and Tau Tangles Present, Cortical Thinning.

The Root Causes of Alzheimer's Disease

1. **Alzheimer's Type 1**- Ongoing Inflammation
2. **Alzheimer's Type 2**- Trophic Support
3. **Alzheimer's Type 1.5**- Glycotoxic
4. **Alzheimer's Type 3**- Toxic Illness
5. **Wild Card**- Homozygous ApOE4 Mutation

In Addition to any chronic disease.

Alzheimer's Type 1

Prolonged elevation in systemic and cellular inflammation degenerates the brain this will in turn begin creating the first AB which can set off the **Prionic** loop imbalance.

Alzheimer's Type 1

Biomarkers:

IL-18

(http://www.cisbio.com/usa/drug-discovery/human-il18-assay-kit)
IL-18 has also been found to increase the Alzheimer's disease-associated amyloid-beta production in human neuron cells.[8]

Hs-CRP

High-sensitivity CRP is thought by some experts to be a useful test for determining risk of CVD, heart attacks, and strokes and that hs-CRP can play a role in the evaluation process before a person develops one of these health problems. Some say that the best way to predict risk is to combine a good marker for inflammation, like hs-CRP, with the lipid profile. Several groups have recommended that this test be used for people who have a moderate risk of heart attack over the next 10 years.

Alzheimer's Type 1

Biomarkers:

Homocysteine

(Huge Link in APP Cleavage and production of AB)
Homocysteine is a chemical in the blood that is produced when an amino acid (a building block of protein) called methionine is broken down in the body. We all have some homocysteine in our blood. Elevated homocysteine levels (also called hyperhomocysteinemia) may cause irritation of th e blood vessels. Elevated levels of homocysteine show an increased risk for (1) hardening of the arteries (atherosclerosis), which could eventually result in a heart attack and/or stroke, and (2) blood clots in the veins, referred to as venous thrombosis.

A/G Ratio (Quest 3293 A)

Albumin to Globulin Ratio: Protein Deficiencies. Can be inverted with liver disease, kidney disease, Inflammatory Bowel Syndrome, Malnutrition, Nutritional Deficiency, Malabsorption, Celiac Disease, amongst others.

Alzheimer's Type 1

Biomarkers:
Cleveland HeartLab®

ADMA/SDMA Ratio:

Elevated ADMA levels are associated with significant subclinical atherosclerosis[1,2] while elevated SDMA levels are associated with impaired kidney function[3,4] and strongly correlate with reduced eGFR.[4]

F2 Isoprostane

The F_2-isoprostane/creatinine is the "gold standard" for measuring oxidative stress and has utility in individuals who have lifestyle risks due to poor diet or smoking, a family history of cardiovascular disease, or hyperlipidemia. High levels are seen in conditions associated with increased risk of atherosclerosis and certain cancers.

Alzheimer's Type 1

Biomarkers:
Cleveland HeartLab®

Lp-PLA2
The Lp-PLA2 Activity assay may be useful for individuals at intermediate or high risk for developing coronary heart disease.

MPO
Myeloperoxidase testing may be used for individuals with multiple risk factors for cardiovascular disease, or those with established disease.

OxLDL
The oxidized LDL test may be ordered for individuals at low or intermediate risk of metabolic syndrome or cardiovascular disease. In addition, this test is useful in individuals who have cardiovascular disease and are at risk for an adverse cardiac event.

Alzheimer's Type 1

Biomarkers:

Gut-Brain Axis

Dysbiotic Bacteria, Klebsiella, Fungal Infections, Parasites, Amoebas.
Increased Gastrointestinal Permeability
Dysbiosis Testing
Comprehensive Digestive Stool w/ Parasitology X1

Oral Hygiene

Elevated Salivary IgA (Diagnostechs)
Periodontal Disease (IFM Questionnaire)
Gingivitis, Extractions, Root Canals, Oral Infections

Chronic and or Recurring Infections-

Viral Patterns Non Proportional Neutrophil to Lymphocyte Ratio (CBC w Differential)
Chronic Allergies, Asthma, Recurring UTI's, Recurring ENT Infections (HX), Etc.

Alzheimer's Type 1

In Addition to any chronic disorder that drives Inflammation in the body:
Meaning patients diagnosed with:

1. Autoimmune Disease
2. Cardiovascular Disease
3. Uncontrolled DM
4. Poor Methylation
5. Poor Detoxification
6. Most GI Disorders
7. Etc, Etc.

Alzheimer's Type 1

There is still much uncertainty about the relationship of inflammation and degenerative brain disease. This line of thinking is only twenty years old and started with the finding that abnormal microglia are involved in brain inflammation and related to degenerative brain diseases.
This question involves very complex research examining the milieu surrounding neurons and synapses, not just neurons. Inflammation outside the brain can, also, affect the brain. Blood brain barriers also appear to be impaired in major degenerative brain diseases.

Research is just now unearthing the great complexity of different kinds of inflammation. Immune cells produce many unique kinds of inflammation for different purposes. Some inflammation can help or hurt the brain after traumatic brain injury. While enormously complex and challenging, this line of research is vital to future understanding of dementia.

Alzheimer's Type 2

Trophic Support-

Is the brain receiving, continuously, all the "things" it needs not only for survival but for optimal function?

What Does the brain need?

How can we test the body to understand the brain?

(Strongest trigger of Antihomestatic Prionic Loops)

Alzheimer's Type 2

Useful Trophic Biomarkers:

Zn/Cu Ratio (Quest Code 945/363)

Highlights

- The serum Cu to Zn ratio is sensible to age related destabilizing events.
- High serum Cu to Zn ratio is associated with mortality in elderly.
- Nutrition, oxidative stress, inflammaging and hormones impact on Cu to Zn ratio.
- Serum Cu to Zn ratio modulates immune defense, growth stimuli and stress response.
- Cu to Zn changes with aging might reflect the attempt of the body to repair itself.

Alzheimer's Type 2

Useful Trophic Biomarkers:

Estradiol & Progesterone

Estradiol and Progesterone are Supportive Factors for the brain of females. Recommended to obtain both Salivary Levels and Circulation.

Testosterone

Testosterone is a supportive factor in the brain of males, drives frontal lobe activation

Alzheimer's Type 2

Useful Trophic Biomarkers:

Thyroid Function Panel
TSH
T4 Total
T4 Free
T3 Total
T3 Free
T3 Uptake
Reverse T3
Thyroid Ab

Glycomark (If Diabetic)
Reveals spikes in blood sugar after meals not identifiable in A1C for FBS
Adiponectin
(C-Peptide in Diabetic)
Asses production of endogenous insulin

Fasting **Insulin** Levels
>7 Represents insulin resistance
A1C -
90 Day average of your Blood Sugar

Lipase
(Diseases of the Pancreas)

LDH
Energy production in the body, also assesses tissue damage

Amylase
Marker low in Diet high in sugar and in diabetes due to pancreatic dysfunction

Total Iron & Ferritin
Iron Storage

Alzheimer's Type 2

Useful Trophic Biomarkers:

Neural Growth Factor

Endogenous Peptide shown to increase neurite extension, instead of neurite retraction. Needs all trophic support present in order to have Epigenetic Expression. Expression is also enhanced by adequate sleep, Regular exercise and proper stress management strategies.

Anemia or Anemia Pattern

If non genetic (i.e.. Thalassemia Major/Minor, Sickle Cell, Etc), improve pattern for better oxygenation to the brain.

VO2Max

Once again oxygenation is key to brain function. Most People have no clue as to what their VO2Max is because they don't know that this value can now be easily obtained.

Alzheimer's Type 2

Useful Trophic Biomarkers:

Nutrition
Key. High level of phytonutrient intake, high fiber, adequate protein and bcaa, high amounts of healthy fats.

Healthy Fasting
Especially in the hours that lead up to sleep.

***Cortisol/DHEA**
(ASI Diagnostechs.com)
Adrenal Dysfunction has been linked to Mental Fog, Mental Fatigue, Depression, Forgetfulness, Hypothyroidism all red flags for Cognitive decline.

Physical Exercise = Brain Food

Alzheimer's Type 2 Trophic

Useful Trophic Biomarkers:

Key Nutrients-
Serum B12
Vitamin D3 25-OH
MCT
Neuronal Structural Components
Good Bugs

Key Functions-

Sharp Mental Focus
Increased SirT1 Function
Frequent/Constant Cognitive Enhancement
Brain Stimulation

Alzheimer's Type 2

Useful **Trophic Biomarkers**:

In other words, anything you feel like it is an important trophic factor for the brain you need to be checking, based on your experience, consistently in every patient.

Alzheimer's 1.5- Glycotoxic

Possesses a combination of elements both from;
Type 1 and Type 2 Alzheimer's meaning:
There are inflammatory changes in addition to Trophic Deficiencies.

Most Common amongst Type 2 (specifically, Insulin resistant Diabetics)

Insulin resistance of the Brain or
(Type 3 Diabetes)

Alzheimer's Type 3- Toxic Illness

Chemicals organic or inorganic, metals and/or toxic organisms will also lead to Neurodegeneration.

Useful Biomarkers for Toxicity-

Mercury Tri-Test (Quicksilver Scientific)
Mercury toxicity has been strongly correlated to neurodegeneration.
Common sources: Organic (Fish consumption), Inorganic (Dental Amalgams)

Comprehensive Blood Metals Test (Quicksilver Scientific)
Of utmost importance in the literature as it refers to Alzheimer's and Prionic Loop disease are; **Lead, Cadmium and Aluminum**

Also of interest are **Lyme Disease and Mold Spore toxicity**.

Alzheimer's Type 3- Toxic Illness

Other common and possible sources of Toxicity:

1. **Multiple exposures to general anesthesia**-
   - Studies have linked multiple toxic insults to the brain resulting from anesthesia to MCI and Alzheimer's Dementia.

2. **Alcoholism**-
   - In large amounts and/or frequent exposures alcohol is a neurotoxin.

3. **Psychoactive Drugs**-
   - Whether legal or illegal, if a drug has psychoactive properties it can create a toxic insult to the brain.

4. **Statins**-
   - Aggressive cholesterol lowering strategies through the use of Statins have been linked with neurodegeneration and Alzheimer's.

Alzheimer's Type 3- Toxic Illness

5. **Poisonous Compounds**

- Whether cleaning products at home or place of work, to intentional poisoning, food poisoning, poisonous creature bites. Poisons in higher than safe limits have the potential to injure neurons. With neuronal injury peptides can be cleaved in a way that they trigger Prionic loops.

6. **Traumatic Brain Injury**

- Some data is suggesting that neuronal death can lead to further neuronal death through Prionic loops and caspase activation.

This area is still not clear, research is ongoing.

7. **Possible Technology and/or EMF Trigger**

-Some data has linked chronic exposure to frequencies emitted from digital devices and the onset of neurodegeneration. (Patient stories)

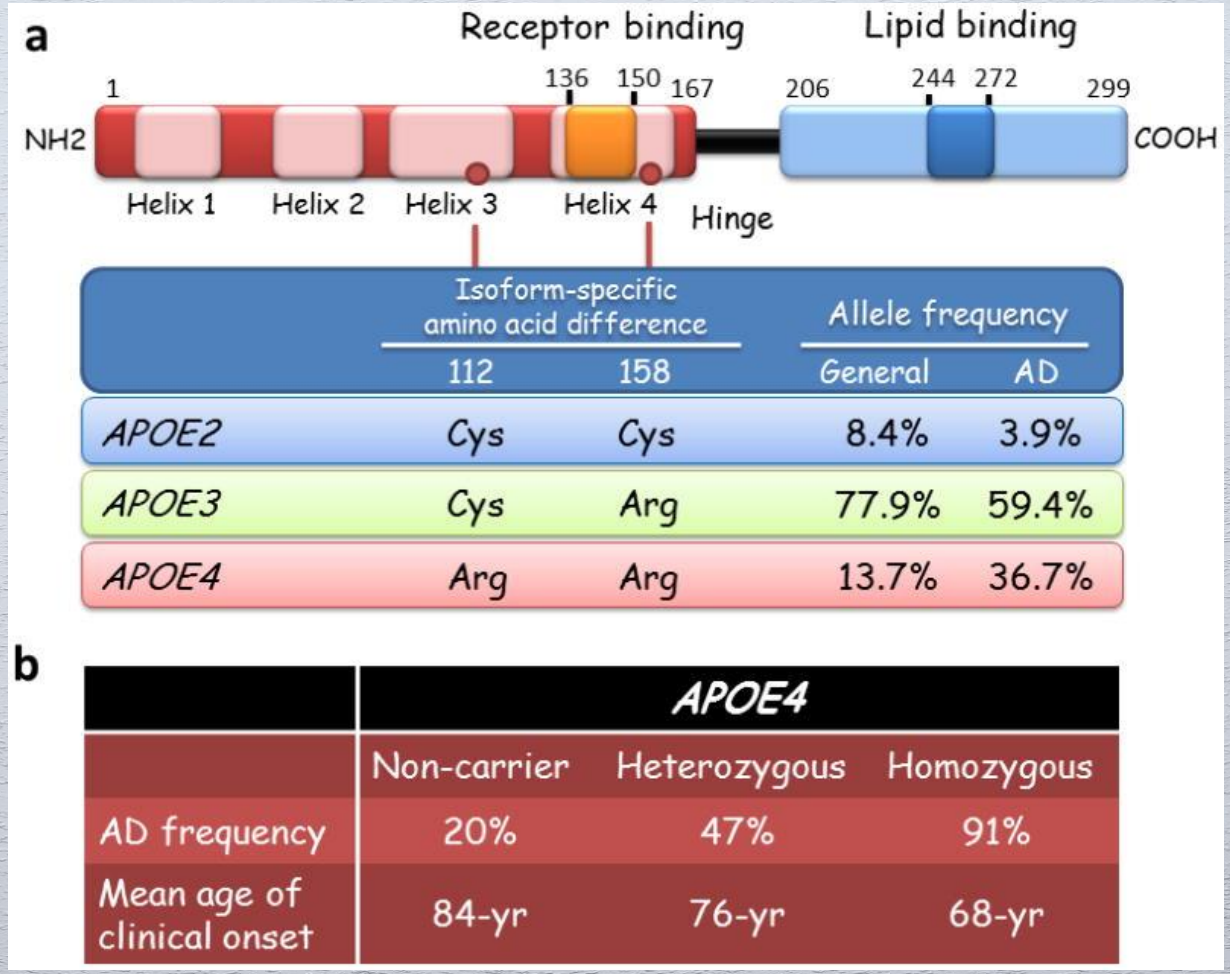
Wild Card ApOE4

Apolipoprotein E (APOE) gene—

A gene on chromosome 19 involved in making a protein that helps carry cholesterol and other types of fat in the bloodstream. It is involved in trophic support and repair for brain tissue. The APOE ε4 allele is the major known risk-factor gene for late-onset Alzheimer's disease.
Presence of the APOE ε4 allele is also associated with increased risk for cerebral amyloid angiopathy and age-related cognitive decline during normal ageing.
ApoE–lipoproteins bind to several cell-surface receptors to deliver lipids and also to hydrophobic amyloid-β (Aβ) peptide, which is thought to initiate toxic events that lead to synaptic dysfunction and neurodegeneration in AD. ApoE isoforms differentially regulate Aβ aggregation and clearance in the brain, and have distinct functions in regulating brain lipid transport, glucose metabolism, neuronal signalling, neuroinflammation, and mitochondrial function

Apolipoprotein E and Alzheimer disease: risk, mechanisms, and therapy

Nat Rev Neurol. 2013 Feb; 9(2): 106–118.

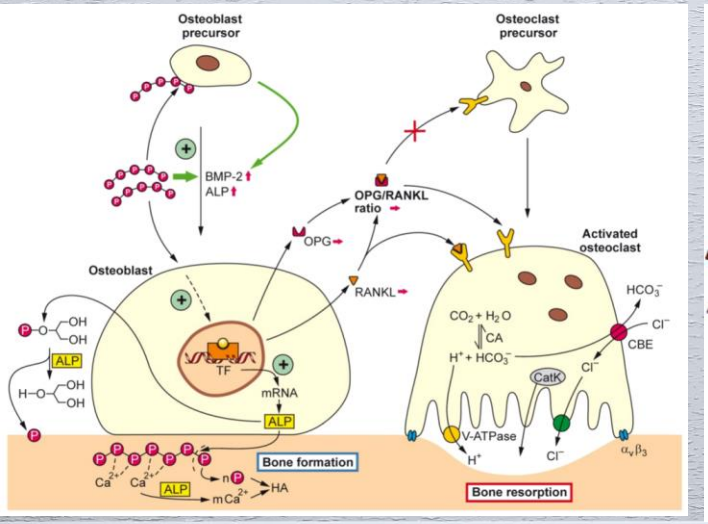

a
Receptor binding
Lipid binding
1
136
150
167
206
244
272
299
NH2
COOH
Helix 1
Helix 2
Helix 3
Helix 4
Hinge
Isoform-specific amino acid difference
Allele frequency
112
158
General
AD
APOE2
Cys
Cys
8.4%
3.9%
APOE3
Cys
Arg
77.9%
59.4%
APOE4
Arg
Arg
13.7%
36.7%
b
APOE4
Non-carrier
Heterozygous
Homozygous
AD frequency
20%
47%
91%
Mean age of clinical onset
84-yr
76-yr
68-yr

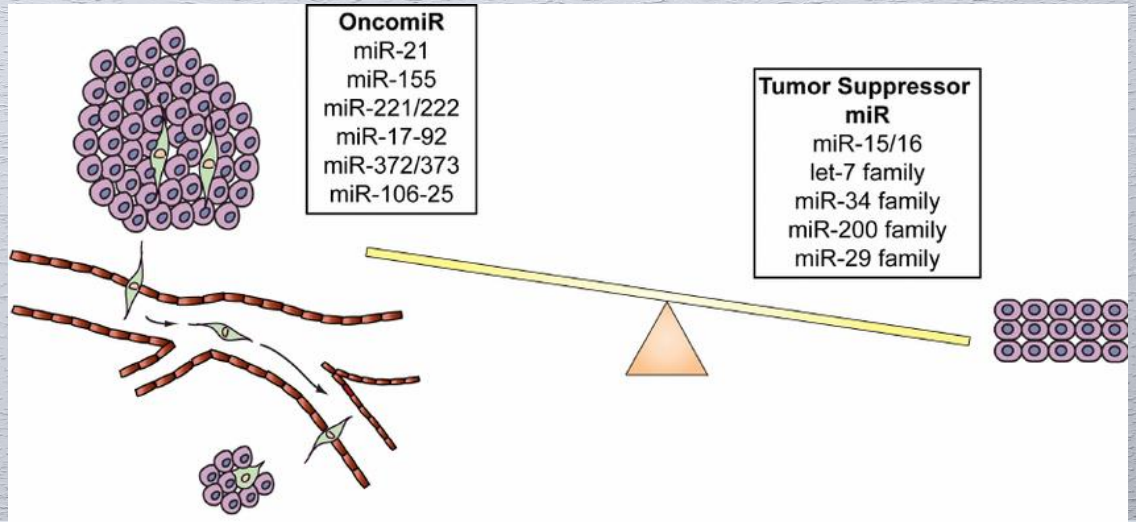
What Are all these mechanisms exactly doing to the brain and how are they connected?

Understanding Balance with Guyton©

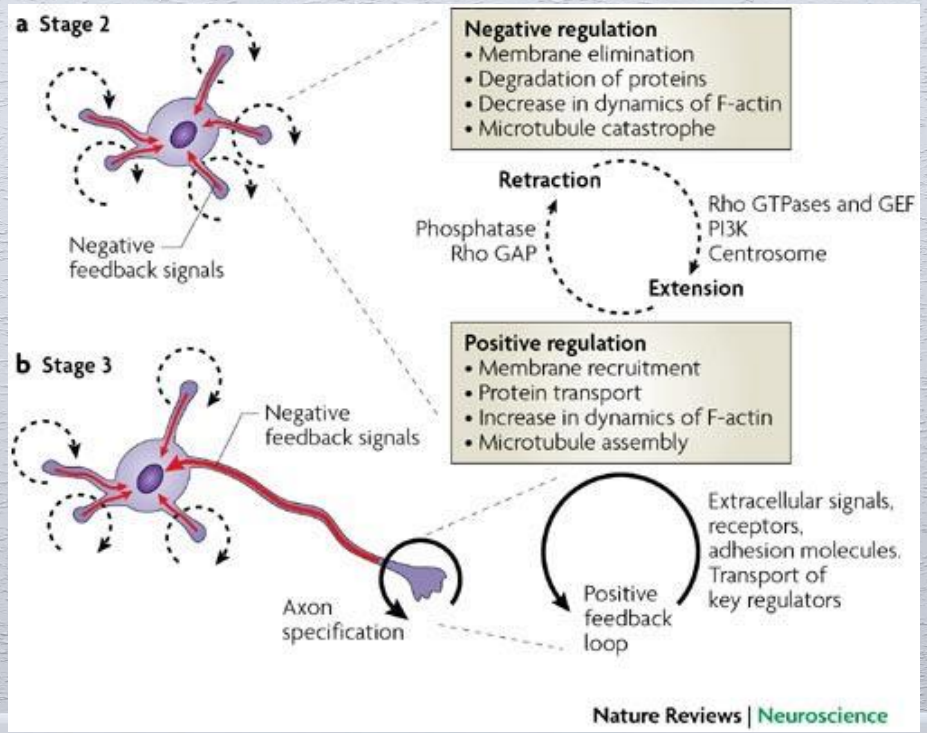
Homeostatic and Anti-homeostatic Loops

Bone **Cancer**



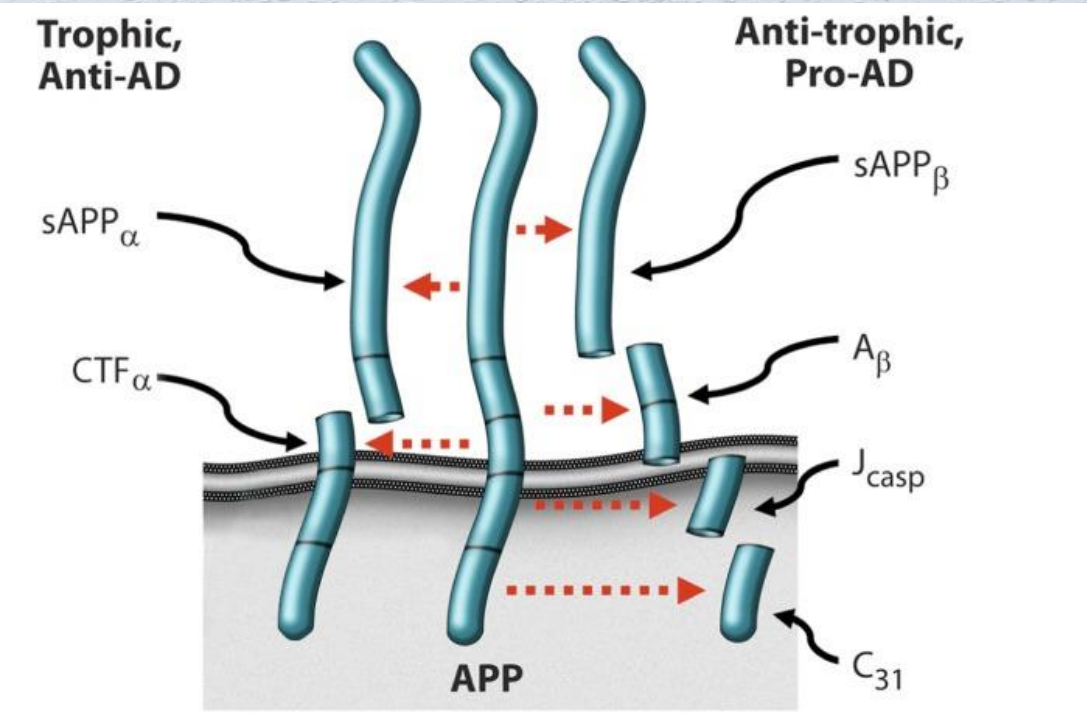


Homeostatic Loops
Molecular Biology of The Brain



Prionic Loops and Caspase Activation

Netrin-1



AB w/ p75NTR

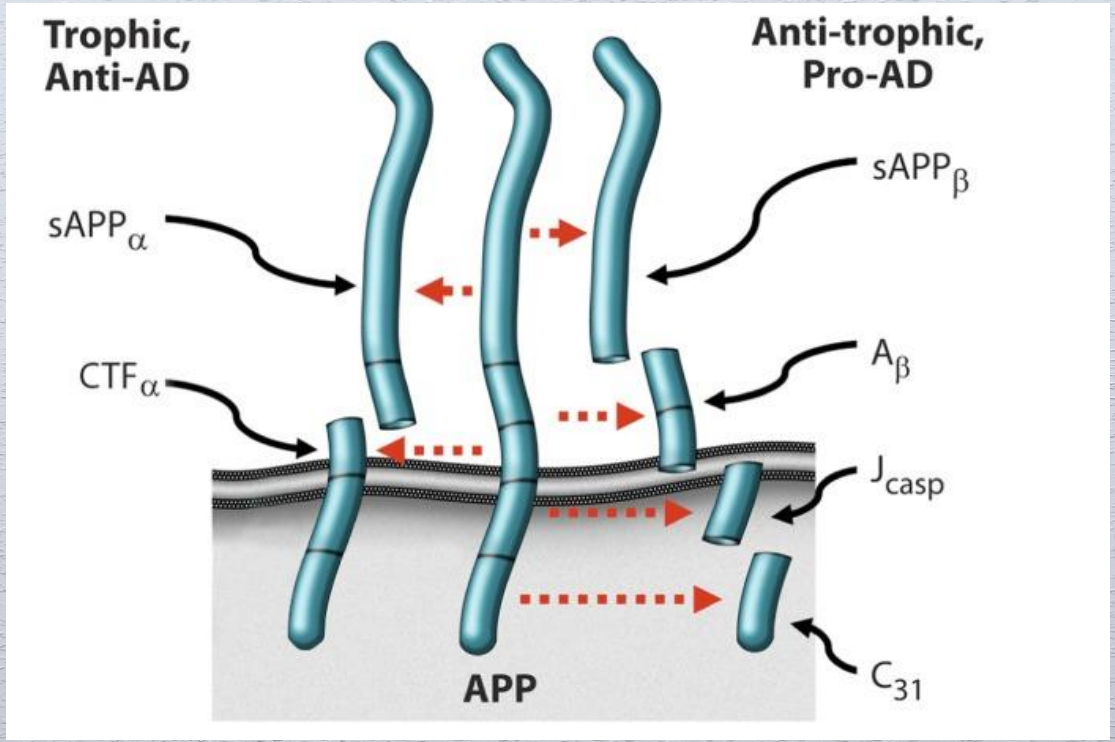
What is the APP Protein?

Amyloid precursor protein (APP) is an integral membrane protein expressed in many tissues and concentrated in the synapses of neurons. Its primary function is not known, though it has been implicated as a regulator of synapse formation,[4] neural plasticity[5] and iron export.

It is the Protein that regulates Neuroplasticity ☺

What Cleaves it and Why?

Netrin-1



AB w/ p75NTR

Acetylaldehyde Dehydrogenase

Enzyme activated from the downstream effects of AB and P75NTR (p75 neurotrophin receptor)

SN- If P75NTR binds to BDNF it will actually have the opposite effect and will increase myelination, solidifying a neuronal pathway.

Monotherapeutics and Issues

Medications in the Pipeline for Inhibition of Acetylaldehyde Dehydrogenase

Disulfiram (Antabuse®)
Possible Analogous Molecules Oxyfedrin and Dyclonine (Sucrets)

Supplementation that could Inhibit Acetylaldehyde Dehydrogenase

Taurine

ISSUES

1. Blood Brain Barrier Permeability
2. Does not Correct the multi factorial dysfunction that is driving the disease, so effect as a monotherapeutic will be minimal at best w/out a functional approach.

LET’S FOCUS ON CAUSE

Protocol (P1)

1. Take Extremely thorough history (this can help determine severity and can help gauge mechanism before testing, perhaps things you want to focus on; (FM TIMELINE is useful)
2. Determine Stage if Patient has been DX with AD (If so try to obtain diagnostic studies. These can be useful in showing objective progress, but not a requirement)
3. Determine if patient is experiencing MCI or Preclinical AD if pt is not yet Dx.
4. Qualify for care:

   Main Criteria

   1. Cannot be undergoing cancer Tx
   2. Cannot have cancer
   3. Co-Morbid conditions that would make it too hard to improve; (MS, Parkinson's, ALS, any other non affective neurological disorder that would mobility and compliance).
   4. Disqualify any advanced or late stage AD patient, in our grading 5, 6 and 7 Always. These patient will not respond to care.
   5. Patients stage 1-3 can be accepted; stage 4 requires a more in depth look.

Protocol (P2)

6. Perform your own evaluation (Mental Status Exam)
7. Perform your own Physical Exam and Include HealthSnap™ Evidence based Assessment.
8. Determine the 4 Following Criteria
    1. Health Goals
    2. Long Term Life Goals
    3. Motivation to Achieve Goals (Both patient's and family members)
    4. Review a list of basic action steps patient will have to handle and determine if patient and family would be willing and motivated to follow recommendations.
9. Accept or Deny Care in your office based on aforementioned criteria.

10. Upon Acceptance, Immediately Order out The Recommended Testing Protocol (MCI TP®)

Protocol (P3)

11. Begin suggested MCI RP® based on findings from the Matrix created from your MCI TP® Protocol.

12. Create a Tx Timeline based on your intake evaluation and your perceived severity of the patient. No protocol should be shorter than 6 months and or longer than 1 year.

13. Inform every patient that based on your findings you will create recommendations that he/she will have to follow for the rest of their lives. Early data is revealing that in patients with remarkable both objective (hippocampal regrowth in volumetric imaging) and subjective (return to work, restored memory and cognition) if they stop their clinical recommendations they will reverse back to a diseased state.

14. Retesting like for any other chronic aliment in a functional model of healthcare shoul d be done every 60-90 days (only those biomarkers that were affected in initial testing a nd that are critical for the patients improvement).

Protocol (P4)

15. Volumetric Imaging is always advisable as a pre and post demonstration of anatomical change in the brain as a result of reversal in the mechanism of the disease. For the longest time the belief was, and still for some physicians is, that brain atrophy is an irreversible pathology. The work being done by Functional Medicine Doctors and Neurologists like Dr. Dale Bredesen is telling a very different story. It seems that the combination of neurite extension and the recent understanding that there are actually stem cells in the connective tissues of the brain, with the proper help and proper stimulation the brain can re-grow.

MCI TP®

Inflammatory
IL-18 (http://www.cisbio.com/usa/drug-discovery/human-il18-assay-kit)
Hs-CRP
Homocysteine
ADMA/SDMA Ratio:
F2 Isoprostane
Lp-PLA2
MPO
OxLDL
A/G Ratio (Quest 3293 A)
Comprehensive Digestive Stool w/ Parasitology X1
For Severe Leaky Gut, Test with Dunwoody Labs
Oral Hygene
(Salivary IgA, Periodontal Disease, Gingivitis, Extractions, Root Canals, Oral Infections, etc.)
Lymphocyte to Neutrophil Ratio
Any other infectious disease

Type III (Toxic Illness)
Quicksilver, Mercury Tri-Test and Heavy Metal Panel
Lyme and Mold Testing
Dysbiosis (Covered already above by DD test)

Trophic Defficiency
Zn/Cu Ratio (Quest Code 945/363)
Estradiol, Estriol, Progesterone
Cortisol/DHEA
TSH
T4 Total
T4 Free
T3 Total
T3 Free
T3 Uptake
Reverse T3
Thyroid Ab
Fasting Insulin Levels
A1C
Lipase
LDH
Amylase
Glycomark (If Diabetic)
Adiponectin
C-Peptide in Diabetic
Ferritin
Iron Storage

ApOE4 Genetic Testing (Cleveland HL)

Labs Needed: Quest/Labcorp, Doctors Data, Diagnostechs, Cleveland Heartlab, Quicksilver Scientific, Dunwoody and a Reference Lab

TREATMENT APPROACH

Goal 1: Reduce Inflammation and Insulin resistance
Optimize Diet, Minimize Simple Carbs, Minimize Inflammatory Foods
(I recommend the Renew Plan, see atachments)

Goal 2: Reduce Insulin Levels, Reduce AB
Enhance Autophagy, Ketogenesis by Fasting 12 hrs every night, including 3 hrs before bed.

Goal 3: Reduction of Cortisol, Corticotrophin Releasing Factor (CRF) and The Stress Axis
Personalized- Stress Reduction Strategies (Yoga Meditation Music Neurofeedback)

Goal 4: Optimize Sleep
8 Hrs Sleep per night. Melatonin 0.5mg and Triptophan 500mg 3x a week if awakening.

TREATMENT APPROACH

Goal 5: Homocysteine <7
Methyl Donors, Me-B12, MTHF, P5P (B6), Trimethylglycine (Amino Acid)

Goal 6: Serum B12>500
Me-B12

Goal 7: HS CRP<1 and A/G Ratio >1.5
Anti-Inflammatory Diet (Renew), Curcumin, DHA/EPA, Optimize Hygiene

Goal 8: Reverse Diabetes
Fasting Insulin <7 and an A1C of less than 5.5

Goal 9: Hormone Balance
Optimize Thyroid, Estradiol, Testosterone, Progesterone, Pregnelonone & Cortisol (Functionally, Adaptogens, HRT, Do what is necessary)

TREATMENT APPROACH

Goal 10: GI Health (Avoid Inflammation and Autoimmune Activation)
Remove (Evidence based antimicrobials, or therapeutics), Repair if necessary and Reinoculate (Pre and Pro Biotics). For difficult cases follow Dunwoody lab protocol.

Goal 11: Reduction of AB
Curcumin and Ashwaganda

Goal 12: Brain Stimulation
Brainess, Posit, Lumosity, etc..

Goal 13: Cognitive Enhancement
Bacopa Monniera, MgT (magnesium-L-threonate)

Goal 14: Vitamin D>55
25 OH D3 Supplementation

TREATMENT APPROACH

Goal 15: Enhance Neural Growth Factor (NGF)
Acetylcarnitine or Hericium Herinaceum (Lion's Mane)

Goal 16: Provide Synaptic Structural Components
Citocoline & DHA

Goal 17: Optimize Antioxidants
Mixed Tocopherols and Tocotrienols, Selenium, Glutathione, Alpha Lipoic Acid, Blueberries, N-Acetyl Cysteine, Ascorbate

Goal 18: Optimize Zn:fCu Ratio
Depends on values obtained supplement accordingly.

Goal 19: Ensure Nocturnal Oxygenation
Apnea? Ensure pt. uses C-pap

TREATMENT APPROACH

Goal 20: Exercise (Brain Food)
For Optimal evidence based recommendations based on patients health status use HealthSnap.

Goal 21:Optimize Mitochondrial Function
CoQ10, Alpha Lipoic Acid, Pyrroloquinoline quinone , N-Acetyl Cysteine, Acetylcarnitine, Selenium, Zinc, Resveratrol, Ascorbate and Thiamine (B1)

Goal 22: Increase Focus
B5-Pantothenic Acid (Acetylcholine Precursor)

Goal 23: Increase SirT1 Function (amongst many can enhance Insulin Sensitivity)
Resveratrol

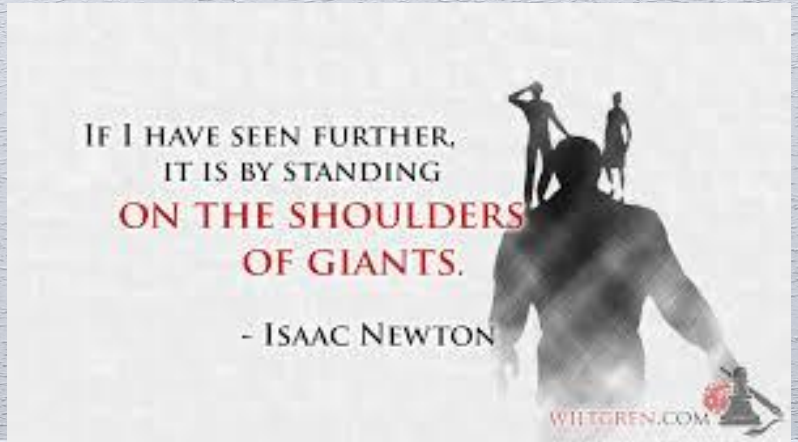
TREATMENT APPROACH

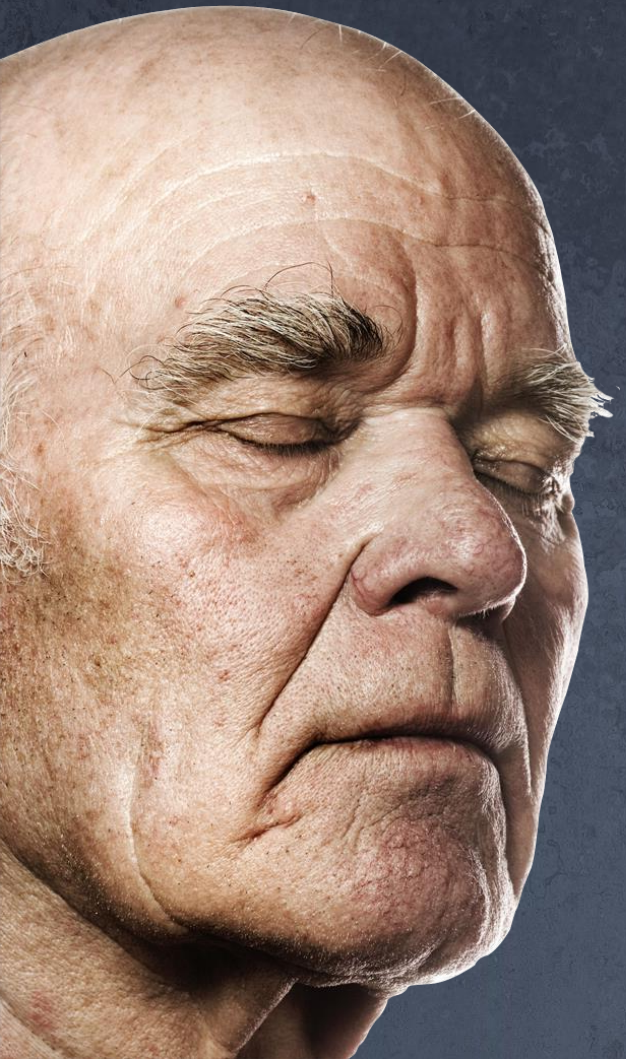
Goal 24: Address heavy Metal Toxicity
I recommend Dr. Shades protocols with quicksilver scientific.

Goal 25: Add in MCT
Coconut Oil or products like AXONA contain Ketones which are the equivalent of "Jet Fuel" for your neurons.

Thank you for your kind Attention
and for all the Amazing researchers and clinicians that have been so aggressively determined to figure out the most complex of all human diseases.

It is an Honor to stand in the Shoulders of Giants as we bring these cutting edge approaches to the masses.





Thank You