ANALYTIC REVIEW

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Clinical Lifestyle Medicine Strategies for Preventing and Reversing Memory Loss in Alzheimer's

Abstract: *Alzheimer's disease (AD) is the most common form of dementia and currently affects over 5 million Americans and 30 million individuals worldwide. Unfortunately, the current approach to treating AD provides nothing more than a marginal, unsustained, symptomatic effect, with little or no effect on disease progression itself. To attain effective improvements in AD, one must determine risk factors, address the underlying causes, and focus on a combination of functional and lifestyle medicine strategies that provide a comprehensive, programmatic, and network-based approach that is sufficient to achieve epigenetic transformation and neurologic healing through its multiple and necessary synergistic components. Rather than normalizing metabolic parameters, the focus is on optimization of each metabolic parameter. Papers published by research neurologist, Dr Dale Bredesen have documented that symptoms of mild cognitive impairment and early AD may often be reversed within 6 months after initiating a comprehensive, functional and lifestyle medicine-focused program. The purpose of this article are as follows: 1. Shed light on a promising clinical protocol that focuses on a comprehensive functional and lifestyle medicine approach to treating mild cognitive decline and Alzheimer's disease; 2. Identify the Bredesen Protocol testing, diagnostic and treatment guidelines; 3. Review several case studies and discuss the promising results of the program. Although published case studies such as those reported here are relatively few, clinicians applying these comprehensive strategies have reason to expect improvement in their patients. Lifestyle medicine can be a source of greatly needed hope for those suffering with cognitive decline.*

Keywords: dementia; Alzheimer's disease; cognitive impairment; lifestyle medicine

Dementia is defined as a decline in mental ability severe enough to interfere with activities of daily living.[1] Based on a variety of studies and research methods, the following staggering statistics shed light on the national and global prevalence and severity of dementia. Of all the various forms of dementia, Alzheimer's Disease (AD) is the most common type and accounts for 60% to 80% of all cases.[1] Currently, 5.4 million Americans and 30

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million worldwide are diagnosed with AD.[2] Of the 318 million people currently living in the United States, 45 million will develop AD. Currently, 40% to 50% of individuals aged 85 years or older suffer from AD. A woman's chance of developing AD is now greater than her chance of developing breast cancer.[3] Additionally, the spotlight on and magnitude of AD has increased with a recent epidemiological report clarifying that AD is now the third leading cause of death in the United States.[4] As of 2015, dementia and Alzheimer's are now reported to be the number 1 cause of death for women in the United Kingdom. Overall, it is also the most common cause of death in men and women older than 80 years.[5] Public Health England reports that life expectancy has increased to 79.5 years for men who can expect to live the last fifth of their life in poor health. Women now live even longer to an average of 83.1 years but can expect to spend "nearly a quarter of their lives in ill-health."[5] Clinicians often hear patients express that they do not want to live a long life because they assume that it will extend the years of dysfunction associated with chronic diseases and, in particular, AD. This, of course, is generally true for those who do not believe in the power of lifestyle medicine to prevent, treat, and oftentimes reverse disease. Fortunately, lifestyle medicine is uniquely suited to guide the aging population of patients who are open to evaluating and broadly addressing the underlying risk factors associated with AD.

Many individuals are under the impression that experiencing "senior moments" and serious mental decline are just a normal part of aging and that there is nothing that can be done to prevent, let alone treat or reverse, cognitive decline. With no current hope for prevention or successful care, those experiencing mental decline tend to delay or even avoid seeking medical attention altogether. Patients who do seek medical care may also avoid disclosing their symptoms to their doctors out of fear of losing their work clearance, drivers' license, or independence altogether.

Why should anyone think differently? So far, conventional medicine has proven to be rather unsuccessful in the treatment of AD, and part of that failure may be attributed to the methods. Currently, conventional medicine treats AD with a 1-step approach, which typically consists of prescribing cognition-enhancing medication such as Namenda and determining the dose regimen. Unfortunately, the current approach to treating AD provides nothing more than a marginal, unsustained, symptomatic effect, with little or no effect on disease progression itself. The main fallacy of the conventional medicine approach to treating AD is that it does not treat the cause of disease, nor does it begin to address the multiple risk factors of AD.

The conventional methods of addressing AD can be compared to the following "thumb tack rules" as postulated by Dr Sid Baker, Professor Emeritus, Yale University School of Medicine. "If you are sitting on a tack, it takes a lot of aspirin to make it feel good."[6] Dr. Baker continues with a corollary:"If you are sitting on two tacks, removing just one does not result in a 50% improvement."[6] But what if someone is sitting on 36 tacks? Only addressing and removing 5 tacks is not going to make the person feel better or provide much improvement at all. The same goes with conventional medicinal approach to AD. If we only address 1 risk factor at a time, there will be minimal benefit, but by comprehensively addressing and treating all known risk factors for AD, clinical experience and research shows that signs and symptoms of mild cognitive impairment and early AD can often be reversed.[2,7]

The field of lifestyle medicine is unique in its ability to meet the demands of the above injunction. What if instead of experiencing fear of a diagnosis or of losing independence, people could experience hope? Norman Cousin's once wrote in his best-selling book, *The Anatomy of an Illness*, "Don't deny the diagnosis, defy the verdict."[8] The goal is to embrace the diagnosis and then develop an aggressive intervention plan.

To attain effective improvements in AD, one must determine risk factors, address the underlying causes, and focus on a combination of functional and lifestyle medicine strategies that provide a comprehensive, programmatic, and network-based approach that is sufficient to achieve epigenetic transformation and neurologic healing through its multiple and necessary synergistic components. To promote optimal health and enable the potential to heal, research neurologist Dr Dale Bredesen has developed a clinical protocol that focuses on a multifaceted approach to treating AD. This protocol aims to provide all the necessary elements that optimize cognition while also removing any of the elements that interfere with cognition.

Studies published by Dr Dale Bredesen and the UCLA Center for Alzheimer's Research have documented that mild cognitive impairment and early AD may often be reversed within 6 months after initiating a comprehensive, functional, and lifestyle medicine–focused program.[7] The basic tenets and themes of the comprehensive therapeutic system often referred to as the Bredesen Protocol include the following[2]:

1. Rather than normalizing metabolic parameters, the focus is on optimization of each metabolic parameter. It is important to understand that laboratory reference ranges typically include values found in 95% of the general public. Having lab values within the reference range, therefore, is not a sensitive or effective standard for health risk assessment. An optimal lab value would be associated with the healthiest individuals within the population and represent those who are least likely to develop Alzheimer's over time.
2. Address the underlying causes of the disease and focus on combination strategies with a comprehensive, network-based, synergistic approach, targeting multiple pathways simultaneously to effect an improvement in symptoms and pathophysiology.

3. Just as in other chronic diseases, the goal is to reach a threshold effect, such that, once enough of the underlying causal network components have been affected, the pathological process would be halted or even reversed.
4. The approach is personalized based on more than 150 data points, including lab testing, scans that include brain magnetic resonance imaging, genomic evaluation, cognitive testing that includes the Montreal Cognitive Assessment, and a detailed medical and family history. The protocol has continued optimization over time. Each network risk factor is addressed in the most rational physiological way and as far upstream in the cause-effect chain, as possible. Lifestyle medicine and clinical nutrition strategies are the core interventional approaches to therapy.

The first and most important component of the Bredesen Protocol is to complete comprehensive laboratory testing and a genomic profile. One of the easiest and most affordable ways to test for Alzheimer's-related gene mutations is to order a Health and Ancestry gene saliva test at http://www.23andme.com. The genomic profile and lab testing assist in revealing the underlying and specific risk factors that over time promote cognitive decline and AD. The Bredesen Protocol encourages a broad evaluation of genetic mutations but specifically analyses the following genes: *ApoE, MTHFR, APP, BDNF, PSEN1*, and *PSEN2*. A patient's tendency to a destructive inflammatory pattern compared with a healing cellular protection pattern is assessed by labs including the following: high-sensitivity CRP; interleukin-6; tumor necrosis factor–α; homocysteine; vitamin B6; vitamin B12; folate; vitamin D as 25-OH-D; vitamin C; vitamin E; omega 6:3 ratio; a comprehensive metabolic panel that includes albumin, globulin, creatinine, blood urea nitrogen, estimated glomerular filtration rate, glucose, calcium, and potassium; NMR LipoProfile that includes the low-density lipoprotein (LDL) cholesterol particle number, small LDL particle number, and LDL size as well as all the components of the standard lipid profile that include total, LDL, and high-density lipoprotein cholesterol and triglycerides; total glutathione; and hemoglobin A1C. Additionally, because insulin resistance is one of the most significant metabolic drivers toward cognitive decline and AD, the Youngberg Clinic includes a 4-hour glucose tolerance test, which also assesses blood levels of insulin at fasting, 1 hour, and 2 hours and assesses cortisol levels at fasting, 3 hours, and 4 hours. Trophic factors, including estradiol, progesterone, pregnenolone, cortisol, DHEA-sulfate, testosterone, free testosterone, and a comprehensive thyroid profile, including thyroid stimulating hormone, free T4, free T3, reverse T3, thyroid peroxidase antibody, and thyroglobulin antibody, are tested and optimized. Additionally, screening for exposure to toxic metals or imbalances of nutrient elements in whole blood is recommended. The elements evaluated with this test are calcium, copper, lithium, magnesium, manganese, molybdenum, selenium, and zinc as well as potentially toxic elements such as arsenic, cadmium, cobalt, lead, mercury, silver, and strontium. Finally, additional lab tests for mold and other biotoxin-related causes of cognitive impairment are also assessed in the Bredesen Protocol.

Once comprehensive genetic and laboratory testing are completed, the Bredesen Protocol promotes a diet composed primarily of whole plant foods, optimizes sleep patterns, personalizes an exercise program, and addresses other factors that when combined together into a comprehensive therapeutic program have collectively produced subjective and objective cognitive improvements in the vast majority of participants.

With more than 150 data points generated by the above screening process, it is possible to complete metabolic profiling and to determine how significantly each of the 6 subtypes of AD is contributing to cognitive decline. By establishing which subtypes are predominant, it is possible to tailor the protocol for each patient. Dr Bredesen summarizes the subtypes below[10,11]:

Type 1, inflammatory. This type is associated with inflammatory markers such as high-sensitivity CRP. The inflammation may be a result of infections, suboptimal diet, or other factors. Risk for type 1 is increased by ApoE4, chronic infections, transfats, and other factors.

Type 1.5, glycotoxic. Type 1.5 has features of both type 1 (inflammatory) and type 2 (atrophic). In this type, chronically high glucose levels damage multiple proteins, cells, and tissues, leading to inflammation and auto-antibodies, all of which increase the risk for type 1 AD. Meanwhile, the responding high insulin levels and associated insulin resistance reduce the trophic effects of insulin and increase risk for type 2. Risk for type 1.5 is increased by ApoE4, type 2 diabetes, and prediabetes.

Type 2, atrophic. This type is associated with especially rapid reduction in trophic support such as estradiol, testosterone, insulin, vitamin D, and neurotrophins. Risk for type 2 is increased by ApoE4, early hysterectomy/oophorectomy without hormone replacement, low vitamin D levels, and in some cases menopause/andropause. It is important to rule out sleep apnea as well.

Type 3, toxic. Type 3 is quite different from types 1, 1.5, and 2, and often presents with features other than (or in addition to) memory loss, such as depression and problems in calculating, organizing, following instructions, or word finding. Type 3 is associated with exposure to toxins (dementogens) such as mercury, high copper levels, anesthetics, mycotoxins

(toxins produced by molds), or tick-related toxins (eg, from Lyme disease). Risk for type 3 is not increased and may even be decreased by ApoE4.

Type 4, vascular. We used to think of vascular disease as being unrelated to AD, but over the past several years, it has become clear that vascular abnormalities contribute importantly to AD. In type 4, chronic vascular disease may be associated with high homocysteine, vascular amyloid, or breach of the blood-brain barrier (among other contributors), and all are associated with the development of AD.

Type 5, traumatic. When the brain is traumatized, for example, as a result of an auto accident, the amyloid associated with AD is produced as a response. Trauma is, thus, a risk factor for AD. In many cases, the amyloid is removed, followed by chronic traumatic encephalopathy. We now know that chronic traumatic encephalopathy is common in football players and in other contact sports as was featured in the film, "*Concussion*." Type 5 typically lacks amyloid but is related to AD in featuring neurofibrillary tangles made of the τ-protein.

Case Study[2]

A 67-year-old female traveling business analyst experienced progressive memory loss for 2 years. She was no longer able to analyze data and prepare reports, had trouble remembering 4-digit numbers, experienced difficulty reading and retaining information, had trouble navigating, had difficulty recalling her pet's name, and had trouble with remembering where light switches were located. The patient had a family history of dementia because her mother developed dementia in her early 60s, which lasted 20 years. The 67-year-old woman was treated with comprehensive testing and encouraged to follow the therapeutic protocol outlined by Dr Dale Bredesen.

Her Therapeutic Program[2]

1. Eliminated all simple carbs
2. Eliminated all processed foods
3. Eliminated gluten
4. Increased fruits and vegetables
5. Underwent a stress reduction program
6. Increased sleep from 4 to 5 hours to 7 to 8 hours per night
7. Took melatonin 0.5 mg at bedtime
8. Took methylcobalamin, vitamin B12 1000 µg daily
9. Took vitamin D3 2000 IU daily
10. Took docosahexaenoic acid and eicosapentaenoic acid 1000 mg daily
11. Took CoQ10 200 mg daily
12. Practiced oral hygiene: electric flosser and toothbrush
13. Reinstated appropriate hormone replacement therapy
14. Had 12-hour intermittent fast between dinner and breakfast
15. Had a minimum of 3 hours between dinner and bedtime
16. Exercised at least 30 minutes for 4 to 6 times per week

In time, all symptoms had abated; she was able to prepare reports and navigate without problem, read and retain information, and remember phone numbers. Overall, she became asymptomatic. She noted that her memory was now better than it had been in many years.[2]

Other Reports

Another patient with well-documented mild cognitive impairment presented with a strongly positive amyloid-PET (positron emission tomography) scan, positive fluorodeoxyglucose PET scan, abnormal neuropsychological testing, and a reduced hippocampal volume in the 17th percentile. After 10 months of following Dr Bredesen's metabolic enhancement for neurodegeneration protocol, the patient experienced an increase from the 17th percentile to the 75th percentile, with a 11.7% absolute increase in hippocampal volume.[6]

From January to December of 2017, the Youngberg Lifestyle Medicine Clinic began working with more than 70 individuals who requested the Bredesen Protocol. Further research is being conducted in coordination with Dr Bredesen, and preliminary results appear to be consistent with Dr Bredesen's published results.[6] Additionally, improvements are being seen in patients who had been diagnosed with AD up to 5 years prior to initiating the program. One patient, in particular, provides profound encouragement to the field of lifestyle medicine. After being told that his AD was incurable and experiencing 3 years of significant cognitive decline, he had lost all hope, which led to depression. Thankfully, his wife chose not to "deny the diagnosis" but rather to embrace it and to "defy the verdict." Through her dedicated research, she discovered the Bredesen Protocol. Prior to starting the protocol in June 2017, the patient was unable to score even 1 point on the Montreal Cognitive Assessment test. Six months later, on December 31, 2017, he was able to score 9 out of 30. More important, after 3 years of significant cognitive decline, his functional capacity to participate in regular, everyday activities improved dramatically. He specifically regained the ability to tie his shoes and dress himself appropriately, participate in social activities with his wife and engage in conversations with others without getting flustered, cook and grill vegetables without burning the food or making a mess, mow the lawn without any missed areas, go shopping without getting lost in the store, and use the microwave without instructions, whereas previously, he had not been able to microwave even with instructions. He now enjoys the ability to control his life. He is pleased with his ability to contribute around the home and be a loving husband to his wife who would not allow him to give up. Few things are more satisfying than to help orchestrate such a reversal of

cognitive decline and to see a husband and wife reunited once again—physically, emotionally, socially, spiritually, and mentally.

In the immortal words of the poet Dylan Thomas, "Do not go gentle into that good night." But rather, "Rage, rage against the dying of the light." There is reason for hope. Although published case studies such as those reported here are relatively few, large studies are in process. Clinicians applying these comprehensive strategies have reason to expect improvement in their patients. Lifestyle medicine may be a beacon of new light that illuminates the journey of health and healing to those suffering with cognitive decline.

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Trial Registration

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