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**AS WE
SEE IT**

Novel Drug Therapy Immediately Reverses Alzheimer’s Cognitive Deficits

By William Faloon

Twenty million Americans alive today are destined to contract Alzheimer’s disease, an affliction that robs us of memory, intelligence, and eventually our most rudimentary cognitive abilities.

Newly diagnosed Alzheimer’s victims are told they will suffer a relentless decline in their neurological function until death. Initial symptoms are short-term memory lapses that worsen until patients cannot recognize their own family members. As dementia progresses, hostile emotional outbursts often manifest, while the patient loses the ability to take care of one’s self—even to the extent of going to the bathroom.

The few drugs approved to treat Alzheimer’s symptoms produce only modest short-term effects. Some patients cannot tolerate them at all.

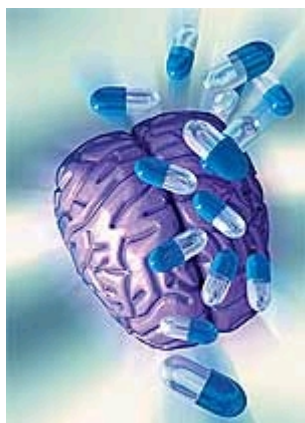
Up until now, a diagnosis of Alzheimer’s meant one was destined to slowly be deprived of all cognitive function—a condition that tops the list of aging people’s disease fears.



William Faloon

BREAKTHROUGH THERAPY RESULTS IN RAPID COGNITIVE IMPROVEMENT

Scientists have linked chronic inflammatory events in the brain with the onset and progression of Alzheimer’s disease.¹⁻¹⁴ A causative inflammatory factor in the neuronal degeneration of Alzheimer’s disease is a cytokine called tumor necrosis factor-alpha (TNF-alpha).¹⁵⁻²²



There are several nutrients that decrease TNF-alpha levels in the body.²³⁻⁴⁵ Ingestion of these nutrients is associated with reduced Alzheimer’s disease incidence.⁴³⁻⁴⁵ For those already afflicted with Alzheimer’s dementia, however, more than just reducing TNF-alpha level is needed to reverse the course of the disease.

In 1998, an anti-TNF-alpha drug called Enbrel® (etanercept) was approved to treat rheumatoid arthritis. Enbrel® does not reduce TNF-alpha in the body. Instead, it functions by binding to TNF-alpha and blocking its ability to latch on to TNF-alpha receptor sites on cell membranes. By interfering with the action of TNF-alpha in this way, the toxic effects of excess TNF-alpha are diminished.

I am going to tell you how Enbrel® can be administered to Alzheimer’s patients in a special way so that it flows directly into the brain, but readers should first understand how TNF-alpha causes senile dementia.

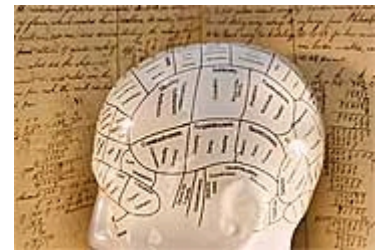
COGNITIVE TEST IMPROVEMENT AFTER SIX MONTHS OF ENBREL® INJECTION

Alzheimer’s Disease Assessment Scale-Cognitive subscale	26%
Mini-Mental Status Examination	12%
Severe Impairment Battery	27%

HOW EXCESS TNF-ALPHA IMPAIRS NEURONAL FUNCTION AND STRUCTURE

In the brain, TNF-alpha can elicit a cascade of cellular events culminating in neuronal death.^{11,46-51} Elevated TNF-alpha has been observed in the brain, cerebrospinal fluid, and serum in Alzheimer’s disease cases.^{2,50,52-54}

Of particular interest is how TNF-alpha affects the “synapses” in our brains. A “synapse” is the point of connection between nerve cells. Brain cells are interconnected and communicate with each other by sending neurotransmitters through the synapses.



Excess TNF-alpha in the brain can disrupt synaptic communication.⁵⁵⁻⁵⁸ A number of findings suggest that synaptic dysregulation caused by excess TNF-alpha contributes to cognitive and behavioral dysfunction in Alzheimer’s disease.^{52,59-68}

Elevated TNF-alpha does more than disrupt vital synaptic communication. A structural change seen in Alzheimer’s disease is the accumulation of amyloid-beta in brain cells. Amyloid-beta accumulation increases inflammation and this inflammation causes further amyloid-beta formation. One mechanism by which amyloid-beta induces inflammation is by triggering an increase in TNF-alpha production.^{60,69-72}

Thus, excess TNF-alpha triggers a vicious cycle whereby toxic amyloid-beta is produced, resulting in greater levels of proinflammatory TNF-alpha, which cause even more amyloid-beta and TNF-alpha formation. Elevated TNF-alpha directly causes synaptic dysfunction and contributes to neuronal destruction. The result of these pathological changes is the horrific senile deficits suffered by Alzheimer’s disease patients.

As you will soon read, the rapid effect of Enbrel® in reversing cognitive impairment helps validate the role of excess TNF-alpha in the debilitating Alzheimer’s disease process.

PROTECT YOURSELF AGAINST EXCESS TNF-ALPHA

A common consequence of “normal” aging is a state of chronic systemic inflammation. This inflammatory state can cause diseases as diverse as atherosclerosis,⁷⁴⁻⁸⁰ cancer,^{81,82} arthritis,⁸³⁻⁸⁷ and Alzheimer’s disease.⁸⁸

Members of the Life Extension Foundation do not intend to age “normally.” To protect against excess proinflammatory cytokines like TNF-alpha, they supplement with nutrients like fish oil,²³⁻³³ luteolin,³⁴⁻³⁷ and curcumin.³⁸⁻⁴² Maintaining a youthful hormone balance using DHEA⁸⁹⁻⁹⁴ and testosterone⁹⁵⁻¹¹⁰ (in men), eating foods cooked at relatively low temperatures,¹¹¹ and sustaining a healthy weight are also critical to suppressing inflammatory reactions.

While Alzheimer’s disease rates are projected to skyrocket with the aging population, a large number of scientific studies reveal that one’s risk can be significantly reduced by eating a healthy diet and taking the proper nutrients and hormones.

HOW ENBREL® IS ADMINISTERED AS AN ANTI-ALZHEIMER’S THERAPY

The approved use of Enbrel® is to self-inject it under the skin once a week to alleviate chronic inflammatory disorders. Enbrel® injected this way, however, will not sufficiently penetrate the blood-brain barrier to produce rapid cognitive improvement.

To deliver Enbrel® to the brain, researchers are injecting it into the back of the neck (in the spongy muscle area between the sixth and seventh cervical vertebrae). The patient’s head is then lowered for about five minutes at a level around their abdomen to better enable the Enbrel® injected into the neck to flow to the brain (through the cerebrospinal venous system).



The dose that had been used in clinical studies was 25-50 mg of Enbrel® in 1 cc of sterile water. Life Extension is exploring the use of Enbrel® in a larger amount of water (2 cc) to enable more Enbrel® solution to travel to the brain.

These Enbrel® injections to the back of the neck (known as interspinous injections) should be administered once a week by a competent neurologist.

THE FIRST PILOT STUDY OF 15 ALZHEIMER’S PATIENTS

Current medical treatments for Alzheimer’s disease do not prevent long-term clinical deterioration.

As discussed, tumor necrosis factor-alpha (TNF-alpha) is a proinflammatory cytokine that is implicated in the neuronal disruption and degeneration observed in Alzheimer’s patients.

An open-label study was conducted in 15 patients with mild-to-severe Alzheimer's disease.²⁰ Three recognized test measures of cognitive function were performed at the study's onset. The patients received weekly Enbrel® injections to the back of the neck, and cognitive testing was repeated at one-month intervals. The following box shows the clinical improvements that were measured in this initial test group after six months:



When one considers that Alzheimer's disease up until now has resulted in worsening of cognitive function, the fact that there was an average 22% improvement in these three mental function measurements after six months is unprecedented.

These patients continued receiving these Enbrel® injections for more than three years. The results suggest that weekly maintenance treatment produces a sustained positive effect, indicating that this novel approach can slow or even halt much of the mental deterioration that occurs in Alzheimer's patients. This again is an unparalleled clinical phenomenon.

SURPRISING FINDINGS REVEAL IMMEDIATE IMPROVEMENT!

The initial studies were limited to measuring the effectiveness of Enbrel® between 30-day intervals. What the researchers and caregivers of these Alzheimer's patients noticed, however, was a rapid clinical improvement within minutes of administering the Enbrel®.

The immediate improvement in cognitive function in these demented patients was unexpected and caught researchers (and their caregivers) off guard. Just imagine how surprising it would be to bring your senile loved one to a doctor's office and observe an instant improvement in their mental function.

The authors of the original study then decided to use several recognized tests to measure the degree of rapid improvement in a new patient treated as part of their standard practice of medicine.



THE SECOND PILOT STUDY

The new patient was an 81-year-old who had been in good general health until about two years before initial presentation, at which time his wife noted progressive memory difficulties and difficulties with mathematical calculation.⁷¹

His wife took over mathematical tasks such as check writing, and the patient was evaluated by a neurologist 18 months prior. The drug Aricept® was prescribed but was not tolerated and was discontinued after four months. Two other Alzheimer's drugs (Namenda® and Exelon®) were prescribed but also were not tolerated by the patient.

A mental status examination performed one day prior to Enbrel® injection into the neck showed this patient had difficulty recalling personal autobiographical information such as his birthday or his father's occupation. He could not recall the names of any of the physicians who treated him. He was not oriented to the calendar date, day of the week, year, place, city, or state. Detailed examination revealed that he had marked difficulty in recalling words, and could not name nine out of 10 pictures he was just shown.

When given a test to measure his linguistic skills, i.e., asked to list all the animals he could in 60 seconds, he could only list two, dog and cat.

On memory testing, the patient could not recall the name of his physician after 90 seconds, despite repetitive introductions on at least four occasions throughout the examination. It took three trials for the patient to register five words and 90 seconds later, the patient could not retrieve any of the words even with categorical cueing.

When asked to draw a clock with the hands placed at 10 minutes after 11, he drew a square without numbers and one line for the hour or minute hand. He could not do a task that involved connecting letters and numbers and was clearly overwhelmed by it.

The patient could not perform simple calculations and could not do serial sevens (counting down from 100 by sevens). When asked to add 29 plus 11 after a marked latency he said 31. Abstract concepts such as a how a train and a bicycle, a watch and a ruler, or music and painting were similar could not be expressed by the patient.

On the Montreal Cognitive Assessment test, the patient scored 7 out of 30 possible points, consistent with moderate-to-severe dementia. Based on these and other cognitive tests, the patient clearly met the established criteria for probable Alzheimer's disease.

SIDE EFFECTS OF ENBREL®

Enbrel® is NOT a drug one would take unless it is critically needed. That is because when administered systemically, it increases the potential risks of infection, low blood counts, lymphoma, demyelinating nerve disease, eye inflammation, congestive heart failure, and death.⁷³ The long-term side effects are not known when Enbrel® is administered primarily to the brain, as is being done in this anti-Alzheimer's treatment.

Written informed consent has been obtained from all these Alzheimer's disease test subjects (or their family members) warning them of these potential risks. The rationale in accepting known and unknown side effect risks is that Alzheimer's disease is a uniformly progressive and lethal disease. There is no other therapy that so rapidly and effectively reverses the clinical course of the disease.

EXAMINATION TEN MINUTES AFTER ENBREL® INJECTION

Immediately prior to Enbrel® injection the patient was questioned by the neurologist. He could not state the year nor could he name the state he lived in.

Ten minutes after Enbrel® dosing, the patient was re-examined. He was noticeably calmer, less frustrated, and more attentive. He was able to correctly identify the state as California, and he identified the year as 2006. His responses to questioning seemed less effortful and more rapid, with less latency. He left to go to a second neurologist for immediate further testing.

FOLLOW-UP NEUROLOGIC EXAMINATION TWO HOURS AFTER ENBREL® TREATMENT

The patient was re-tested by another neurologist two hours after Enbrel® administration. While he could not recall being in the treating neurologist's office earlier in the day (before the Enbrel® injection), he did recall the name of the second neurologist he was seeing. He was now oriented to month, day of week, and place, and could again correctly name the state as California, which he could not do prior to Enbrel® injection to the back of his neck. He was off on the calendar date by two days, and the year by one year.

The patient's ability to name pictures was markedly improved, correctly naming nine out of the first 10 pictures, a marked improvement from the day prior when he could only name one of the 10 presented pictures. On the verbal fluency test, he was able to list eight words that started with the letter "F" in 60 seconds and made only one erroneous response. On a linguistics task, he was able to list five animals in 60 seconds.

On visuospatial functioning, the patient could copy a three-dimensional cube, and when asked to draw a clock, he drew a circle with an hour and minute hand. When given a test to connect letters and numbers, the patient was clearly able to sequence and complete the task, alternating letters and numbers accurately. He was able to pantomime seven out of eight finger constructions of increasing complexity.

On memory testing, the patient could not recall any of five memoranda after five minutes even with categorical cueing. With multiple-choice cueing, he could recall one out of five memoranda. However, he could recall the examiner's name without difficulty and without necessity of repetition of introductions throughout the entire examination.

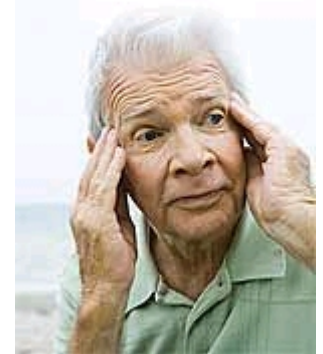
On attentional testing, the patient could accurately list five digits in a forward fashion and three digits in a reverse sequence fashion. On a vigilance task test, he made no errors of omission or commission.

On calculations, he could subtract seven from 100 correctly, but could not perform serial sevens. He could not divide 58 by two, nor could he add 29 plus 11. He could not tell the neurologist how many nickels were in a dollar.

On ability to abstract concepts, he was able to relate how a train and bicycle were similar in that they both can be used for transportation. When asked how a watch and a ruler were similar, he related that they both give information. When asked how music and painting were similar, he related, "You draw your painting; however, music you hear."

Montreal Cognitive Assessment performed two hours following the single dose of Enbrel® injected into the back of his neck, yielded a score of 15 out of 30 points... a 115% improvement compared with the previous score of 7 before the Enbrel® injection (only two hours before).

A collateral interview with the patient's son and wife confirmed their validation of a marked improvement in cognitive abilities



following Enbrel® administration

NEUROLOGICAL EFFECTS ONE WEEK AFTER INITIAL ENBREL® INJECTION

Upon returning for his second weekly Enbrel® injection, the patient's wife and son confirmed that he had remained markedly improved throughout the week.

He was less reluctant to join in conversation. On re-examination by the first neurologist prior to receiving the second weekly dose, the patient correctly identified the year, month, season, day of week, and state. He appeared to answer with less frustration, and the examiner's impression was that there was reduced latency of response, along with other observable improvements. On the test for verbal fluency, when asked to list all of the words that start with the letter "F" in 60 seconds, he listed eight words and named five animals in 60 seconds.

SUSTAINED IMPROVEMENT

The patient received a single dose of Enbrel® injected into the back of his neck for each of the first five weeks; the next dose was omitted, and the patient returned after seven weeks for retesting. At this seven-week interval (and 14 days after receiving his last dose of Enbrel®), his Montreal Cognitive Assessment score was 14 out of 30 (a 100% improvement from the baseline score of 7), with persistent improvement in the numbers-letters connecting task, and improved depiction of the clock face.

The researchers stated that the rapid cognitive improvement following Enbrel® injection to the back of the neck is not limited to this patient. It had in fact been commonly observed in multiple patients during these researchers' more than three years of clinical experience utilizing Enbrel® for treatment of probable Alzheimer's disease.^{20,71}

LIFE EXTENSION FOUNDATION HELPS VALIDATE FINDINGS

In as much as these clinical improvements are unprecedented, the Life Extension Foundation conducted a pilot study of a 91-year-old female Alzheimer's disease patient who suffered severe cognitive deficits.

There was immediate improvement after the first Enbrel® injection. For example, she was able to follow simple commands such as "tap your fingers" that she couldn't do before the injection. She was more animated as well.

After four weeks, the results on the Mini-Mental Status Exam showed a significant 150% improvement, and her aid described her as engaging in more accurate discussions and eating better.

The family of this Alzheimer's patient and the treating neurologist noticed an immediate improvement after the first Enbrel® injection. According to her son, who is a medical doctor:

"My mother is doing better. Her conversations are longer. She is asking to go for walks outside. She is no longer incontinent of stool. When I told her I was going to give a talk in Boca Raton next month she said, "I am very proud of you." She has not said anything that complex in years."

Life Extension is continuing to fund this patient's Enbrel® therapy and follow up on her progress. Regrettably, due to complications related to her advanced Alzheimer's disease state, administering these weekly injections has been challenging. Every effort is being made to help this woman regain some of her cognitive abilities. Future studies will be aimed at early-stage Alzheimer's disease patients.

NEW CLINICAL STUDY SPONSORED BY THE LIFE EXTENSION FOUNDATION

Based on these extraordinary findings, the Life Extension Foundation is seeking to launch an expanded study with the objective of measuring the long-term effects of weekly Enbrel® injections plus nutrients that help suppress the production of excess TNF-alpha.

Enbrel® is an extremely expensive drug. The normal cost of the Enbrel® and weekly injections is approximately \$675. If you or a person you know with early-stage Alzheimer's disease desires to participate in this new clinical study, there will be no charge for treatments.

The study site will be in south Florida. Since the Enbrel® injections will have to be administered weekly, study participants should ideally reside in the Fort Lauderdale area.

Due to the potential side effects of Enbrel®, there are bureaucratic hurdles we have to comply with before initiating this formal

study. Once we have institutional approval, Life Extension will initiate this study aimed at validating a proven method to reverse Alzheimer's disease. We hope to keep the delay in launching this study to a minimum, but many of the regulatory aspects are beyond our control.

To inquire about enrolling in this new study sponsored by the Life Extension Foundation, call 1-866-517-4536.

A NEW ERA...

In 1907, Dr. Alois Alzheimer performed an autopsy on the brain of a deceased individual and noted the structural characteristics of the disease that now bears his name. Up until now, there has been no effective way to slow this horrific condition.

For the first time in medical history, those afflicted with Alzheimer's disease may enjoy an immediate reversal of cognitive deficits, while potentially slowing the destruction to their precious neurons caused by TNF-alpha-induced inflammatory reactions.

Up until now, taking a loved one to a doctor's office and learning of an Alzheimer's disease diagnosis meant a bleak future of unrelenting neurologic decline. Based on what has been discovered, newly diagnosed patients may soon gain access to these special Enbrel® injections and enjoy a rapid and long-lasting restoration of cognitive function.

For longer life,



William Faloon

If you have any questions on the scientific content of this article, please call a Life Extension Health Advisor at 1-800-226-2370.

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