



A publication for friends and donors of Alzheimer's Disease Research

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Drug That Can Slow Progression of Alzheimer's Disease Approved

Memantine Considered Major New Treatment for Alzheimer's Patients

A drug synthesized originally in 1963 as a potential agent for lowering blood sugar levels (it failed miserably) has now resurfaced four decades later as a major new treatment for Alzheimer's disease.

Memantine (pronounced Me-MAN-teen) is the first drug approved in the United States and Europe for the treatment of moderate-to-severe Alzheimer's disease and the first drug to slow the progression of the disease.

Though far from being a cure, memantine is able to prolong the period that Alzheimer patients can take care of themselves and the period before they need to be put in a nursing home. As a result, memantine is expected to save the U.S. economy over \$13,000 a year per Alzheimer's patient.

Part of the disease process in Alzheimer's disease is the

overstimulation of nerve cells, or neurons, in the brain by a messenger chemical, or neurotransmitter, called glutamate. Glutamate is an amino acid that is prevalent in protein. In the brain, glutamate is the main neurotransmitter that excites neurons, particularly neurons that are involved in learning and memory. When something important happens in the environment, some neurons release large amounts of glutamate, which stimulate

other neurons involved in learning and memory. In this way, the brain notes the important event and makes a memory of it.

The problem in Alzheimer's disease is that there are constant low levels of glutamate floating around in the brain, continuously stimulating neurons, even when nothing notable is happening outside the body. This creates a lot of noise in the brain's learning system, such that when something important happens, the neuronal signals noting this get buried in the noise.

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For more information on projects being funded by Alzheimer's Disease Research, visit us on the web at: www.ahaf.org



President's Corner

With your help, hope is on the rise

More than 4.5 million Americans are believed to have Alzheimer's disease and by 2050, the number could increase to 13.2 million. As a result of increased life expectancy, Alzheimer's disease is on the rise ...

But as a result of your generosity, so is hope for a cure.

Since Alzheimer's Disease Research (ADR) was established in 1985, we have awarded more than \$46.9 million to support promising research — some of which is outlined in this issue of **Alzheimer's Research Review**. The fact is, we are advancing against Alzheimer's disease, both in prevention and in the march toward new treatments and a cure.

I hope you take great satisfaction in the progress that your contributions make possible. With your continued support, there is no doubt that we will find the cure that is the dream of millions of Americans.

Brian K. Regan
 Brian K. Regan, Ph.D.
 President

New Treatment Approved

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This is apparently why Alzheimer patients have trouble learning new facts and remembering old ones. Their brains are just too “noisy” to function properly.

To make matters worse, all this glutamate stimulation increases the amount of calcium inside neurons. Some calcium is needed for normal neuronal function and memory formation, but too much calcium sets into motion processes that end in the destruction of the neuron. This is partly why large sections of the brain die off in Alzheimer's disease.



Memantine works by blocking the constant stimulation of neurons by low levels of glutamate. This dampens down the noise in the system and prevents excess calcium from accumulating inside neurons. Now when something important happens and some neurons release high levels of glutamate, neurons receiving the glutamate signal

can detect it. No longer does the signal get lost in the noise. As a result, the brain of Alzheimer patients can function more normally.

In animal studies, memantine was shown to improve learning and memory in aged rats and improve memory in rats missing a part of the brain that is affected in the early stages of Alzheimer's disease.

In clinical trials of memantine for treating Alzheimer's disease, the drug was shown to reduce declines in mental functioning, improve behavior (for example, reduce agitation), and reduce the burden on caregivers.

In one study, patients who received memantine were three times more likely to remain independent after 28 weeks than those given a placebo.

More drugs are being developed for Alzheimer's disease that attack different aspects of the disease process and several are currently in clinical trials. In the meantime, memantine remains a major player in the treatment of Alzheimer's disease.



Is it Alzheimer's . . . or Not?

Five conditions that can mimic Alzheimer's disease

Grandpa had been acting a bit strange lately. First, he started having problems remembering directions when he was driving and wound up getting lost every time he went to a place where he had never been before. Then, he began forgetting the names of simple objects, such as a toothbrush or a hammer. The family really started getting worried when they realized that he could no longer balance a checkbook and had forgotten what an ATM card was.

They wondered: was this the beginning of Alzheimer's disease?

People with Alzheimer's disease experience a gradual loss of memory and mental capacity. However, a variety of other, often treatable conditions can cause similar symptoms, and distinguishing between these disorders and Alzheimer's is not always easy.

The more families know about the symptoms of these

disorders and those of Alzheimer's, the more they can help physicians make the correct diagnosis and prescribe the proper treatment.

DEPRESSION

Early Alzheimer's disease shares much in common with depression. People with Alzheimer's often become apathetic, giving up their hobbies and even losing interest in friends and family. On the other hand, depressed people may experience memory loss, appear disoriented, and perform poorly in tests of intellectual function, all of which are characteristic of dementia.

However, depression, as opposed to Alzheimer's, generally has a sudden onset, often precipitated by a serious emotional event. In tests of intellectual function, or cognitive ability, depressed patients may perform poorly but realize this and complain about it, whereas Alzheimer's patients are oblivious to their poor performance. Also, Alzheimer's patients eventually show obvious cognitive

abnormalities — such as difficulty in telling left from right, loss of the power of expression, and inability to copy drawings — while these capabilities remain intact in depressed patients.

STROKE

A stroke, or interruption in the supply of blood to the brain, can cause multiple areas of the brain to die, often causing symptoms similar to Alzheimer's disease. Dementia due to a stroke is called multi-infarct dementia.



Unlike Alzheimer's, which progresses steadily, multi-infarct dementia has a sudden onset and fluctuates with periods of improvement and deterioration. Also, multi-infarct patients often have problems walking, sometimes

shuffling and even occasionally walking backwards involuntarily. Brain imaging can be useful in detecting areas of coagulation and dead brain tissue, which can help distinguish multi-infarct dementia from Alzheimer's.

VITAMIN DEFICIENCIES

Vitamin B12 deficiency affects 10 to 15 percent of people over 60. The problem is almost always caused by reduced absorption of the chemical in the small intestine. Mental disturbances range from mild irritability and forgetfulness to severe dementia or psychosis. Vitamin B12 injections stop the disease process and improve mental functioning.

STRUCTURAL BRAIN ABNORMALITIES


A structural brain abnormality can include a brain tumor, chronic subdural hematoma (blood that accumulates just outside the brain due to a closed head injury), and arteriovenous malformation (tangled masses of blood vessels in which blood flows directly from arteries into veins without first passing through capillaries). These abnormalities sometimes put



pressure on the brain in such a way as to cause Alzheimer-like symptoms. These structures can be easily detected in brain images and treated through radiation or operations.

SEXUALLY TRANSMITTED DISEASES

Syphilis, in its last or tertiary stage, can mimic Alzheimer's disease. This can occur as much as 20 years after the initial infection. Syphilis can be easily diagnosed using various blood tests and treated, even in its late stages, with penicillin or other antibiotics. HIV infection can also cause dementia, and in some patients, dementia is the first sign of the infection.

For more information about Alzheimer's disease, see the American Health Assistance Foundation website at <http://www.ahaf.org> or call 1-800-437-2423. 

Research Update

Thanks to you, research is making advancements against Alzheimer's disease


As you know, Alzheimer's Disease Research (ADR) funds dozens of projects each year, focusing on some of the most innovative research around the globe. We have highlighted just a few ADR funded projects which are making significant progress against the disease, thanks to your generous support.

At the Max-Delbrueck Center for Molecular Medicine in Berlin, Germany, M. Olav Andersen, Ph.D is searching for a way to stop the breakdown of “plaques” — the dense deposits of proteinaceous material that are toxic to nerve cells — which

are a hallmark of the brain in Alzheimer's disease. His research has already identified a novel protein in nerve cells that seems to play a role in the breakdown.

Oxidative stress plays an important role in age-related conditions such as Alzheimer's disease. However, the effects of oxidative stress in the living brain with Alzheimer's disease have not been clearly described. The objective of In-Young Choi's research at the University of Kansas Medical Center is to measure a molecule in the brain called Glutathione (GSH) — which will lead to a

better way of evaluating the effects of antioxidant therapy in patients with Alzheimer's disease in the future.

Identification of the genes related to Alzheimer's disease is one of the most challenging tasks neuroscientists need to address in order to understand the disease — and find a cure. Using a technology known as Laser Capture Microdissection (LCM) Huaxi Xu, Ph.D. at the Burnham Institute in La Jolla, California, is seeking to isolate individual types of neurons in the brain region that controls cognitive activity. The potential result? An increased understanding of the molecular mechanisms underlying pathogenesis of Alzheimer's — and the opportunity to develop effective therapies. 

Exercise Your Brain to Fight Alzheimer's Disease

New study shows that mental activity can minimize the risk of dementia


Research from the University of New South Wales (UNSW) provides convincing evidence that complex mental activity significantly reduces the risk of dementia. **The researchers found that such activity almost halves the incidence of dementia.**

The paper, published in *Psychological Medicine*, is the first comprehensive review of the research in the field of ‘brain reserve’, which looks at education, occupational complexity and mentally stimulating lifestyle pursuits in preventing cognitive decline.

“It is a case of ‘use it or lose it,” said the lead author, Dr. Michael Valenzuela, from the School

of Psychiatry at UNSW. *“If you increase your brain reserve over your lifetime, you seem to lessen the risk of Alzheimer's and other neurodegenerative diseases.”*

The key conclusion is that individuals with high brain reserve have a 46 percent decreased risk of dementia, compared to those with low brain reserve. All the studies assessed agreed that mentally stimulating leisure activities, even in late life, are associated with a protective effect.

“This suggests that brain reserve is not a static property, nor that it is determined by early life experiences such as level of education, socio-economic deprivation or poor nutrition,” said Dr. Valenzuela. *“It is never too late to build brain reserve.”* 

Adapted from the following source: University of New South Wales

Planned Giving

Leaving a Lasting Legacy

Many of our most faithful donors want to do more than simply make an occasional gift to Alzheimer's Disease Research (ADR) — they want to play a major role in finding a cure! One of the most effective ways to do that is by leaving a contribution to Alzheimer's Disease Research in your will.

If you don't have a will, your first step is to contact a lawyer or estate planner and have them assist you in drawing one up. When you do, we hope you will consider leaving a bequest to Alzheimer's Disease Research which will allow us to continue

our vital investigations on behalf of those with Alzheimer's disease. If you already have a will, you can simply add language that includes a gift to ADR.

Have questions? Would you like more information on planned giving? Please contact Gayle Handiboe, Manager of Development, at gandiboe@ahaf.org or 1-800-437-AHAF and thank you for thinking of Alzheimer's Disease Research!



www.ahaf.org

Simply click on the Alzheimer's Disease Research link to learn more about what's new in the world of research, as well as important information about risk factors for Alzheimer's disease.

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