

Alzheimer's Disease - In Pursuit of a Cure

This is an exciting time for Alzheimer's disease research. Over the last decade, great progress has been made, and there is no doubt that major breakthroughs are on the horizon.

The Alzheimer Society of Canada is a leading funder of Alzheimer research and research training in Canada, contributing close to \$30 million in the past 20 years. In 2008, the Society and its partners funded over \$2 million in support of both Biomedical and Quality of Life research fields.

The fact remains that there is currently no cure for Alzheimer's disease. More funding must be given in support of Canada's researchers, who rank among the top Alzheimer scientists in the world.

What is Alzheimer's Disease?

Alzheimer's disease is a progressive and degenerative brain disease that destroys memory, reasoning, orientation in time and place, along with other cognitive functions. Alzheimer's disease is not a normal part of aging.

In Alzheimer's disease, multitudes of dense, irregular microscopic spots or plaques develop all through the brain, and thread-like tangles appear within the brain cells. The toxic effects of these changes cause nerve cells to degenerate, especially those involved in memory and cognition. However, it seems that it takes years for the sick nerve cells to die, offering hope for new treatments to intervene and promote their recovery.

Biomedical Research

Biomedical researchers are working to try and understand exactly how the adverse changes are brought about in the Alzheimer brain, with the end goal of designing treatments to prevent their development. As well, they are actively following a variety of approaches to promote brain repair that will compensate for the damage that has occurred, perhaps even restoring "lost" memories, which may still exist in the brain, but have become inaccessible.

New Therapies

The principal target of Alzheimer's disease therapy is still beta -amyloid (A-beta), the protein which accumulates in the brain and eventually deposits in the form of microscopic amyloid plaques. These particles, a major hallmark of Alzheimer's disease, are scattered throughout the brain outside the nerve cells, and are regarded by many, including Dr. Alzheimer himself more than 100 years ago, as the principal culprit responsible for the degeneration and eventually the death of the brain's nerve cells. A prominent current theory is that the accumulation of A-beta is also responsible for the other major hallmark of Alzheimer's disease, the fibrous tangles seen inside the nerve cells themselves.

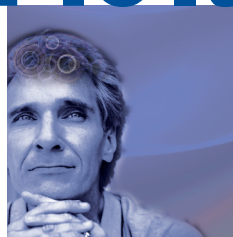
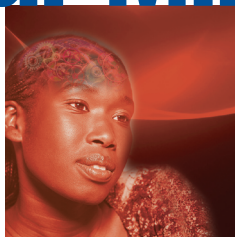
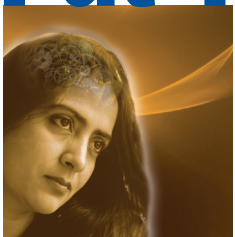
Tangles are composed of a protein called "tau" which has become abnormally altered chemically in the cells. These snarled bundles of fibres which build up inside the nerve cells in the brains of people with Alzheimer's disease may well be the immediate cause of the nerve cell's dying, because the tangles interfere with the normal critically important movement of chemicals inside the cells and along the nerve fibres that emanate from the cells.

The 2008 International Conference on Alzheimer's Disease (ICAD) presented 20 promising treatments that are currently in clinical trials. Although still at a very preliminary stage of development, examples of new exciting drug therapies include: PBT2; which opposes A-beta production, and has been shown to improve the brain function of people in early stages; Rember, a drug which is showing an 81 per cent improvement in the rate of mental decline; and AL 108, a drug administered by way of a nasal spray.

An Alzheimer Vaccine

There are promising developments in the search for an Alzheimer vaccine. The first attempt, which showed positive results with mouse models of the disease, was halted early in the first phase of human trials in 2002 due to the development of brain inflammation in some participants.

Put Your Mind To It



New vaccines anticipated not to cause inflammation of the brain are very actively being designed, and at least three are in early clinical trials.

In one new approach, instead of giving substances which will stimulate the production of antibodies (active immunization), already manufactured antibodies are provided directly (passive immunization). Finally, a new experimental vaccine has been created which targets one of the key enzymes involved in splitting the toxic A-beta from its big parent protein.

Early Diagnosis

It has long been hoped that biological 'markers' for Alzheimer's disease would appear in various tissues that could be more easily studied than the brain itself. New findings are offering hope that early diagnosis could be considerably assisted by such biological markers. Recent reports described two such markers in the skin of people with Alzheimer's disease: firstly an abnormal inflammatory chemical response that is easy to detect; and secondly, the presence of abnormal levels of a number of proteins.

Risk Factors

Alzheimer's disease appears to be caused when the combined effects of many risk factors, including age, genetics, lifestyle and environmental factors, overwhelm the natural self-repair and self-healing mechanisms in the brain. To this end, an increasing amount of research is focusing on learning more about these risk factors for Alzheimer's disease, on what people can do to reduce them, and also on ways to enhance the brain's self-healing capacity.

Other Areas of Research that could Lead to New Treatments

1. **Promoting brain repair:** Even when a truly successful treatment for Alzheimer's disease appears, there will still be a need to deal with the damage already caused in the brain. Of great importance here is a class of substances called 'growth factors', which promote the health of nerve cells and their ability to grow new connections with other nerve cells. One critically important growth factor is called the nerve growth factor, or NGF. Studies, which are testing its potential in people with Alzheimer's disease, are showing initial promise both at keeping nerve cells from dying and for improving cognition.
1. **Alzheimer's disease and diabetes:** Research shows that, even when diabetes in the conventional sense is absent, anti-diabetic drugs called glitazones can help maintain brain function in people with Alzheimer's disease. The continued testing of these drugs is based on the idea that, in people with Alzheimer's disease, there may actually be a sort of diabetes of the brain. This

idea is supported by the observation that when insulin was administered through the nasal passage of people with Alzheimer's disease (this approach gets the insulin preferentially to the brain without going through the rest of the body), memory and cognition improved in some cases – a promise of future therapeutic measures.

3. **Stem cell research:** A persisting problem in stem cell research has been how to obtain the substantial number of stem cells needed for research. Two recent research reports have cast new light on the situation. Using a 'retrovirus' as an infecting agent, certain molecules known as 'transcription' factors were introduced into fully developed human skin cells. Genes were activated that converted adult skin cells back into an earlier and more primitive state, into cells in fact that closely resembled normal embryo-derived stem cells. The excitement generated by these reports was not just because of the discovery of how to transform normal adult cells into stem cells, but because of the implication that stem cells could now be obtained without the involvement of human fetuses. Likely it will be decades at the very least before we have a viable stem cell replacement therapy.
3. **Statins:** Cholesterol-reducing agents, called statins, are continually being tested because of earlier discoveries that they can lower the abnormally increased levels of A-beta protein found in the Alzheimer brain. Statins could thus be safe and effective ways to slow the progression of Alzheimer's disease.
3. **Cognitive rehabilitation:** In this therapeutic approach, people with Alzheimer's disease are subjected to a variety of repeated memory and other cognitive testing procedures by trained psychologists. The results are a marked slowing in the progression of the disease.

For a more in-depth look at current research in Alzheimer's disease, please visit www.alzheimer.ca and download *A Report on Alzheimer's Disease and Current Research*.

Quality of Life Research

Researchers in the social and psychological fields are working to identify the personal, social and environmental factors that affect people with Alzheimer's disease, with the hope of improving caregiving techniques, and enhancing the quality of life for both the person with the disease and their caregivers. The Alzheimer Society of Canada was recently given a special donation to create a research award focused on music and dementia that explores the therapeutic benefits of music on people with Alzheimer's disease or a related dementia.

For more information contact:
www.alzheimer.ca or 1-800-616-8816