

# GERONTO-McGILL

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## A Satisfying Social Life Can Lessen Dementia Risk

by Jeff Boyczuk

The intangible benefits of close relationships with family and friends are obvious, but as you age these relationships may provide the additional advantage of warding off dementia. This suggestion comes from a recent study on the relationship between social networks and dementia occurrence from Lisa Fratiglioni and colleagues from the Stockholm Gerontology Center<sup>1</sup>.

The researchers followed a group of 1203 elderly Swedes over a 3-year period. At the outset, all were living at home and performed well on tests of mental functioning. Participants were questioned extensively about their relationships with family and friends. By the end of the study period, 176 participants had developed cases of dementia, the majority being of the Alzheimer's type.

The data showed that the highest rates of dementia were found among those participants who had the least extensive social networks. Being married proved to be the single most protective factor. Those who were widowed, divorced, or lived

*(Continued on page 2)*

### IN THIS ISSUE

SOCIAL LIFE AND DEMENTIA	1
REVERSING NEURON CELL DEATH	1
FOCUS ON ALZHEIMER'S DISEASE	1
ALZHEIMER AND ESTROGEN	4
SEEKING HELP FOR HOME CARE	5
AGING-RELATED WEBSITES	6

## MISSION POSSIBLE: REVERSING NEURONAL CELL DEATH

The research of Dr. Andrea LeBlanc, Associate Professor, Department of Neurology and Neurosurgery, McGill University, and Project Director, Lady Davis Institute of the Jewish General Hospital

by Hannah Hoag

"From the beginning I thought that if I was going to study Alzheimer's disease (a disease that is virtually unique to humans) and if neurons were implicated, I'd better look at human neurons". Seven years later, the perseverance of Dr. Andrea LeBlanc is unflinching and causing a stir in the community that studies the relationship between neuronal cell death and Alzheimer's disease.

LeBlanc is a recently tenured Associate Professor in the department of Neurology and Neurosurgery at McGill University and a Project Director at the Lady Davis Institute. Although her research focus has changed significantly since her post-doctoral days at the Mayo Clinic in Rochester, Minnesota, she remains passionate about her work and its challenges. The goal of



her work is to uncover a method of preventing neuronal cell death, so that it might be used to develop treatments for Alzheimer's disease.

*(Continued on page 2)*

## PUBLIC LECTURE SERIES

### Alzheimer's Disease: today, tomorrow

by Alison McTavish

Alzheimer's Disease was the topic for the 10th anniversary presentation of the McGill Centre for Studies in Aging (MCSA) public lectures. Three speakers provided a packed conference room at the Montreal Delta Hotel with an overview of the current understanding of the disease as well as a look at treatment options and future research.

Dr. Judes Poirier, Director of the MCSA, explained Alzheimer's risk factors, and Dr. Serge

Gauthier, Director of the MCSA Alzheimer Disease Research Unit, discussed the latest therapeutic options. Julie Bélanger, a specialized consultant at the Alzheimer Society of Montreal, told the audience about the help that's available in the community for both patients and families.

#### Dr. Judes Poirier: Who is at risk?

Among those who develop Alzheimer's Disease, 10% to 15% are genetically predisposed while 85% of cases are sporadic. In addition to the

*(Continued on page 3)*

## A Satisfying Social Life Can Lessen Dementia Risk

(Continued from page 1)

alone showed an increased occurrence of dementia.

Fratiglioni et al's findings also pointed to quality over quantity in social relationships, with the frequency of social contacts mattering less than the satisfaction level in relationships that were maintained. For instance, participants who seldom saw their children but enjoyed positive contacts with them showed less susceptibility to dementia. The effect also worked in the opposite direction, with elderly individuals who had frequent but poor interactions with their children showing an increased occurrence of dementia.

How can positive social contacts lower the incidence of dementia? The authors speculate that emotional and intellectual stimulation reaped from such relationships may delay or compensate for the pathological alterations and cognitive decline that is known to precede the onset of a clinical diagnosis of dementia. Furthermore, they note that previous research has shown that poor social networks may weaken the immune system. Dementia, which is partially characterised by inflammation in the brain, may progress more rapidly under such conditions. While both of these suggestions are highly speculative, the findings from the current study clearly warrant further investigation of the relationship between social isolation and the occurrence of dementia in the elderly.

<sup>1</sup> Fratiglioni L, Wang H, Ericsson K, Maytan M, Winblad B. Influence of social network on occurrence of dementia: a community-based longitudinal study. *The Lancet* 2000;355:1315-1319. ■

## MISSION POSSIBLE: REVERSING NEURONAL CELL DEATH

(Continued from page 1)

LeBlanc's approach to studying Alzheimer's disease differs from that of her peers. She has developed primary cultures of human neurons to use as a model system for her research. Although unique, this approach is well devised. Early in her career, LeBlanc realized that human and rat neurons were likely to display inherent differences. Primarily, she questioned whether the lifespan of rodents precluded their utility in a disease that affects the elderly. "You're born with most of your [central nervous system] neurons, and you will live with them for about 80 years on average... you can't reproduce [this lifespan] in a rat neuron or a mouse neuron". The primary cell cultures of human neurons that she has devised live up to the characteristics of their in vivo counterparts. These cells are hardy: "they survive many insults, they're strong – they want to survive". And this resilience is precisely what LeBlanc wants to study.

The neuronal model allowed LeBlanc and her colleagues to determine that human neurons do behave differently than cultured rat or mouse neurons. These differences, she says, have made her theories somewhat controversial and not always accepted by her peers. Most researchers use mouse or rat neurons in their studies and LeBlanc's results do not always concur with those of her peers. "It is often difficult to get our results accepted... our system is unique and these neurons do not always behave as rat neurons do". However, her thorough and meticulous approach to research has led to the gradual acceptance of her ideas.

One of these ideas is that the initiation of apoptosis is the driving force in the pathogenesis of Alzheimer's disease. The brains of patients with Alzheimer's disease are riddled with senile plaques that are composed of 2 forms of amyloid-beta peptide. Since LeBlanc hypothesizes that these plaques form after the apoptotic cascade has started, she focuses her research on the upstream processes and mediators of the cell death cascade.

Cellular commitment to apoptosis is mediated by a series of cysteine proteases called caspases. Caspase activation causes the cell to become irreversibly committed to apoptosis.

Activated caspases cleave certain proteins that are essential to the integrity of the cell, and ultimately lead to the destruction of the cell. One such caspase target is the amyloid precursor protein. LeBlanc has determined that activated caspases are capable of cleaving the amyloid precursor protein into the fragments that are found in plaques, showing that the induction of caspase-mediated cell death directly influences the metabolism of the amyloid precursor protein.

In addition, LeBlanc has singled out a mammalian caspase and implicated its intimate involvement in human neuronal cell death. By micro-injecting primary cultures of human neurons, one of LeBlanc's graduate students has shown that human neurons are especially susceptible to apoptosis when it is initiated by a caspase called caspase 6. Interestingly, under certain conditions, the actions of caspase 6 can be inhibited, permitting the human neuron to escape "irreversible" cell death. Estrogen is one agent with the ability to hamper neuronal apoptosis after it has been initiated.

Epidemiological studies have observed that postmenopausal women who receive hormone replacement therapy carry less risk of developing Alzheimer's disease than untreated women, suggesting that estrogen may protect against the development of Alzheimer's disease. LeBlanc decided to test that theory on her human neuronal cell cultures and showed that "estrogen acted as a neuronal protecting agent against caspase 6 mediated [neuronal] cell death". Soon after, the laboratory isolated a protective factor from estrogen-treated human neuron cultures. Once it is characterized, this caspase inhibitory factor (CIF), which is specific to human neurons, "could be a good target for the treatment of all types of neurodegenerative disease".

Although LeBlanc is not currently involved in the treatment of Alzheimer's disease, her accomplishments prove that that could change in the future. To date, no drug has been developed that can treat the loss of neurons that is observed in Alzheimer's disease. Although some pharmaceutical companies are developing chemical agents that act as caspase inhibitors, their targets are non-specific; they affect multiple cell types of the brain. The problem with this

(Continued on page 3)

## MISSION POSSIBLE: REVERSING NEURONAL CELL DEATH

(Continued from page 2)

approach in preventing neuronal cell death is that drugs that target both neurons and astrocytes (cells that do divide), for example, may prevent neuronal cell death, but may also promote astrocyte tumorigenesis. As such, companies are taking notice of LeBlanc's research. Compounds that upregulate the expression of neuron-specific CIF could be used to prevent neuronal cell death in the brains of individuals with neurodegenerative disease, without promoting the proliferation of other types of brain cells.

Bit by bit, LeBlanc is chipping away at the mystery of Alzheimer's disease and enjoying the associated challenges. While musing over her accomplishments and the frustrations associated with research, she concludes: "I don't think I could have chosen a better career for myself". ■

## PUBLIC LECTURE SERIES

### Alzheimer's Disease: today, tomorrow

(Continued from page 1)

known genes that pass the disease directly in a small number of families, researchers have identified a few genetic mutations that greatly increase risk in some families.

Of particular interest is the apolipoprotein E (apo-E) gene. Dr. Poirier explained that the normal memory loss that occurs as we age starts earlier for people with two copies of the apoE-4 gene and relatively later for those with one or no copies of the gene. Genetic testing for apo-E is currently possible, but it is not widely available because it has little predictive value. Despite the increased risk of developing Alzheimer's that results from having two apo-E4 genes, not everyone with the genes will develop the disease.

A relatively new finding is that high blood pressure places those aged between 30 and 40 at high risk for developing Alzheimer's later in life. Dr. Poirier emphasized the importance of hypertension treatment for this group to help reduce their risk. Contrary to popular belief, the aluminum found in products such as antiperspirants and Alka Seltzer does not appear to be a risk factor for disease development.

Dr Poirier noted that several things appear to be protective against Alzheimer's. People with a higher education appear to be less at risk, although it isn't entirely clear whether this is a result of associated socioeconomic factors, or because of the increased mental agility that comes with higher learning. Additional studies have shown that non-steroidal anti-inflammatory drugs, antioxidants (such as vitamin E and Ginkgo biloba) and red wine also appear to be protective.

Although it has been speculated that cigarette smoking and post-menopause estrogen supplements may also help reduce the risk, Dr. Poirier pointed out that recent, large clinical studies have refuted this.

#### **Dr. Serge Gauthier: New treatment options**

Dr. Gauthier opened his talk by discussing the different phases of Alzheimer's. He noted that the order in which symptoms appear is important for diagnosis.

The disease often begins with a period of unexplained depression that eventually resolves. Cognitive ability begins to decline, followed by functional autonomy. Behavioral changes are profound, but eventually settle down. Physical decline occurs in the final stages of the disease. Families are often faced with the difficult decision of whether to place the patient in a nursing home as the physical decline worsens.

Dr. Gauthier went on to point out that new treatment for the disease is offering hope for sufferers and their families. Dr. Gauthier explained the importance of the neurotransmitter acetylcholine in the progression of the disease: Alzheimer's patients have a 50% decline in acetylcholine levels. Ameliorating this decline with acetylcholinesterase inhibitors is the goal of therapy with new drugs for Alzheimer's treatment.

Acetylcholinesterase inhibitors prevent the breakdown of acetylcholine resulting in more effective use of the little that is available. Dr. Gauthier illustrated that patients treated with Aricept, currently available in Quebec, experienced significant reductions in apathy, anxiety and depression, and were able to retain their autonomy for a longer period. Patients treated with Aricept often spontaneously return to activities they once enjoyed doing but had stopped. Exelor, a newer drug that was available in Quebec as of October 1st, and galantamine, a drug soon to be approved in Quebec, are similarly effective.

Unfortunately the therapies available today are not able to cure Alzheimer's. The delay of disease progression is relatively short term and deterioration among treated patients is eventually parallel to deterioration among patients left untreated. Future therapies will be aimed at stopping disease progression entirely.

#### **Julie Bélanger: Support is available**

The last speaker of the day was Julie Bélanger, a specialized consultant at the Montréal Alzheimer Society. Bélanger discussed the impact of the disease on families and told the audience what to expect when a loved one develops Alzheimer's.

(Continued on page 4)

## Estrogen and Alzheimer's disease

by Farzad Saberi

Dementia is a progressive mental disorder characterized by defective problem solving skills, memory and judgement. Alzheimer's disease (AD) is the most common cause of dementia, found in 60-80% of cases. It affects twice as much women as men. AD is mainly a disease of the elderly, estimated to occur in 5-15% of people over 65 years old. This disease is a major cause of morbidity and mortality, and a tremendous cost to the health care system. Recent years have witnessed the introduction of many treatment options for this disease, including medications such as Aricept, hormone replacement therapy (HRT), fish oil, and even vaccination against the protein that accumulates in Alzheimer's disease brains.

There are many reasons as to why HRT has become an attractive option for the treatment of AD. In laboratory rats whose ovaries were removed surgically, thus providing an animal model for postmenopause, estrogen was found to improve their ability in certain memory and cognitive tasks. In addition, estrogen was found to improve neuronal growth in the brain, and interestingly neuronal survival after an experimentally induced stroke in these animals. All these results suggest that estrogen confers an improved function and survival on neurons. Even in healthy postmenopausal women, estrogen has been shown to have beneficial effect on mood and verbal memory. In children with Turner syndrome (females who do not produce adequate amounts of estrogen), it has been shown that exogenous estrogen improves skills on certain cognitive functions.

Experiments and clinical trials in AD patients however have not yielded the same promising results as in animals. A few studies with small numbers of women have shown a beneficial effect of estrogen in preventing or delaying the onset of AD. These results were questioned because it was also shown that those women using HRT were more educated and were from a higher socioeconomic class, both factors protecting against AD. Three large controlled studies are currently underway that are looking at healthy postmenopausal women and they should answer the question regarding the effect of HRT on the prevention and/or onset of AD. The completion of these studies is however a few years away. This year has been witness to three moderately large and well-designed studies that have looked at the effect of HRT, from 3 months to 1 year in

(Continued on page 5)

## PUBLIC LECTURE SERIES

### Alzheimer's Disease: today, tomorrow

(Continued from page 3)

The disease is particularly hard on caregivers, and Bélanger outlined the common signs of caregiver stress. Denial, she pointed out, is a common first reaction. There must be a mistake; this can't be happening to our family. Often caregivers become angry with the patient and begin to withdraw socially because they are afraid to leave the patient alone at home and are afraid that friends won't understand. Anxiety, depression and sleeplessness are common. Ultimately caregivers become exhausted and develop health problems of their own.

How can the Alzheimer Society help? The society, said Bélanger, assists not only those suffering from the disease, but also families and caregivers. Services for patients include an activity centre, social club and support groups for patients in the early stages of the disease. While dealing with an uncertain future, these patients are often afraid of becoming a burden to their families and are trying hard to remain active and independent.

Because so many Alzheimer's patients have wandered from their homes and forgotten their addresses, the society offers a wandering registry. Patients are given an identification bracelet that advises the person who finds the patient to call the local police. Police are then able to quickly trace the family via a national database that contains information on family members to contact.

Services for family members include individual counseling, support groups, a support line and quarterly information bulletins. Bélanger emphasized that the general public can also use the numerous books and videos in the society's documentation centre, and can call the local help and information line.

#### Resources

Alzheimer Society of Canada

<http://www.alzheimer.ca>

(English and French)

Fédération québécoise des Sociétés Alzheimer

<http://www.cam.org/fqsa>

(French)

Montreal chapter:

5165 Sherbrooke West

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Telephone: (514) 369-0800

Fax: (514) 369-4103

Email: [samasm@qc.aira.com](mailto:samasm@qc.aira.com) ■



## Estrogen and Alzheimer's disease

(Continued from page 4)

duration, on women who already are suffering from AD. Unfortunately none of these studies have shown an improvement in this condition with estrogen. Some have proposed that the chronic effect of AD on the brain is irreversible and will not respond to estrogen. The mode of treatment has also been questioned, since laboratory experiments have shown a greater effect of estrogen when administered as intermittent pulsatile rather than continuous treatment. In addition, some have argued that the level of estrogen required to obtain the desired effect needs to be found.

The bottom line is that our knowledge regarding the effect of estrogen for the treatment of AD is still controversial. We know that estrogens are beneficial in postmenopausal animal models. We also know that estrogens have little or no effect when given to patients who are already suffering from AD. The remaining important question to be answered in the future is if estrogen can prevent or delay the onset of AD in healthy postmenopausal women. There is optimism that the answer to the latter question will be positive, since it is

believed that estrogen preferentially affects and protects younger, healthier brains rather than those affected with AD.

### References:

- 1) *Neurology*. 54(11): 2035-7, 2000 Jun 13.
- 2) *JAMA*. 283(8): 1055-6, 2000 Feb 23. ■

## POLICY AND POLITICS

### Seeking Help for Home Care *by Jeff Boyczuk*

For some, an unfortunate circumstance of old age is needing assistance with daily activities such as eating and washing. While institutionalisation is one solution to this problem, patients in this predicament more often than not prefer to receive care at home. Under the current health care system, such an option is not always possible.

In May of this year, the National Advisory Council on Aging (NACA) released a report entitled *The NACA Position on Home Care*. The report contains a series of recommendations to federal and provincial governments directed at making home care an integral part of the current and future Canadian health care system. The report continues 20 years of NACA advocacy for the development of a national home care system. Today, more than ever, this issue is critically important.

The current demand for home care services in Canada is not being met. The 1998 National Population Health Survey revealed that of 136,000 respondents who required assistance with daily activities such as dressing and eating, less than half actually received formal home care service. This under-served population, comprised mainly of senior citizens, is instead forced to turn to costly private home care services or family and friends for assistance.

The situation is only likely to grow more dire in the coming years as baby boomers and their parents age. A recent study by the Canadian Heart and Stroke Foundation indicated that more than two thirds of the baby boomers are currently in a poor position to cope with a parent who

requires home care assistance. Respondents indicated that they were either inflexible in adjusting their work hours to personally provide care for a parent, that they could not handle the psychological stress of living with a parent who required daily assistance, or that caregiving would be a financial burden. Nevertheless, as noted in the NACA report, it is inevitable that a large proportion of baby boomers will assume the responsibility for home care as their parents grow older.

Currently, home care costs are absorbed by many parties, including provincial and municipal governments, insurance companies, and the care recipients themselves. A concern in what seems to be increasingly for-profit trend in home care is that private companies will target their services towards large-volume profitable sectors, leaving low-volume rural areas under-served. The NACA proposes that a public system with a single payer be put in place. This would both reduce administration costs associated with tracking multiple payment sources, and promote equivalent levels of care for all regions of the country.

Realistically, even with a comprehensive public home care system in place, family and friends of care recipients will still play a fundamental role in the process. The NACA report recognises this, and recommends support for these "informal" caregivers. Specific recommendations include making provisions in the Canada Pension Plan (CPP) for a drop-out period in which people who have temporarily left the work force to care for a relative are not penalised in the ultimate calculation of their CPP

benefits. Such a provision currently exists for those who take a leave from work to care for their children. The report also recommends investigating the plausibility of extending Employment Insurance (EI) benefits to those who must temporarily leave work to assume caregiving responsibilities.

The inevitable concern about the cost of establishing a publicly funded home care system arises, given an already strained health care budget. In fact, a 1999 Canadian study has shown that costs for home care may be one half to three quarters that of equivalent care provided in public facilities. Consequently, a simple payer public home care system may have the double-barrelled benefit of increasing the comfort level of care recipients and, at least in the long run, easing the financial burden on taxpayers.

While the NACA rightly acknowledges federal government initiatives over the last two decades in making home care a priority, clearly more progress on the issue is needed. The current situation, in which thousands of seniors are not receiving the home care services they need, will only grow worse in the coming years as the proportion of seniors in the Canadian population grows.

*The NACA Position on Home Care* may be found at :

[http://www.hc-sc.gc.ca/seniors-aaines/pubs/naca/naca20\\_e.htm](http://www.hc-sc.gc.ca/seniors-aaines/pubs/naca/naca20_e.htm) ■

## REGISTRY OF AGING-RELATED WEBSITES

by Farzad Saberi



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#### Alzheimer's Association website

[www.alz.org](http://www.alz.org)

A very well designed and simple to use website, provides information on latest research and medical developments on Alzheimer's disease. It also includes information for caregivers, and social aspects of this disease. This site even includes employment opportunities for patients, unfortunately they are in the US only.

#### Alzheimer's conference 2000

[www.alzheimer2000.org](http://www.alzheimer2000.org)

This is the website describing the first global conference on Alzheimer's disease, held in July 2000 in Washington, DC. This conference gathered scientific, social, and professional experts from around the world. This site explains the latest developments in this field presented at this conference.

#### Search engine watch

<http://www.searchenginewatch.com/>

This site lists and rates (for coverage) search engines. It has a section called Specialty Search Engines which includes a list of Medical Search Engines. Here are some sites in that list :

#### MedHunt

<http://www.hon.ch/MedHunt/>

MedHunt is maintained by the "Health On The Net" (HON) foundation. It has an English and a French interface.

#### Biocrawler

<http://www.biocrawler.com/>

This is a biological search engine — from anthropology to zoology...

#### Medical World Search

<http://www.mwsearch.com/>

Covers medical sites and uses a thesaurus of medical terms to look for related pages.

#### 9-11.com

<http://www.9-11.com/>

This site maintained by the California Public Safety Academy is directed at consumers, medical practitioners, and researchers.

#### Accumedinfo

<http://www.accumedinfo.com/>

Another search engine dedicated to medicine. It searches through medically-oriented web sites.

#### CiteLine.com

<http://www.citeline.com/CISE/search>

Searches through a pre-screened index of medical sites.

#### Univers Santé

<http://www.generique.net/pages/>

Search engine for the French speaking scientific and medical community (in French).

#### Galenicom

<http://www.galenicom.com/>

A search engine of medical resources on the net in Spanish.

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