The Foundation Newsletter

THE SCOTTISH RITE
CHARITABLE FOUNDATION OF CANADA

EDITION No. 19 OCTOBER 2004

President's Report

Success stories, new challenges in our 40th year

In this, the 40th anniversary year of The Scottish Rite Charitable Foundation, I have the opportunity to look back at the success of the past and look forward to an exciting, but demanding, future. Thanks to our donors, the Foundation has been able to grant millions of dollars over the past 40 years to researchers and students who are looking for solutions to mental challenges in children and the elderly. As with all research, progress on diseases such as Alzheimer's, is slow and methodical. But the research we support is making headway and we are proud to be part of the relentless march toward effective treatments.

2003-04 was an exciting year in three ways. First, the London Centre for Children took in its first group of students and from all accounts, it was a terrific success. Second, the participation rate for donations to the Foundation increased to 6.6% from 6.2% last year. Third, some $500,000 was distributed through the tireless work of the Grants and Awards Committee to persons throughout Canada searching for causes and seeking solutions to the puzzles of the mind in the young and the elderly.

However, challenges remain. Quite simply, if we are going to do more we will need to raise more money.

It's human nature to be attracted to the new, and certainly the London Learning Centre, as our newest venture attracted its share of attention. Already there is an informal waiting list of parents who want to enroll their child and there are more volunteers coming forward to be tutors.

My favorite story concerning the Centre focuses on one young girl, who, after just six months of tutoring, increased her reading skill by three years. It's a story like this that makes our work, and our donations, so satisfying. I can imagine the smile which must have spread across her face, and across the face of her parents; and how future prospects have brightened for that family.

I thank London Valley for their initiative and for their exceptional work culminating in the dedication of the Learning Centre in the Masonic Temple on May 16, 2004.

Another initiative of the Learning Centre Committee was the introduction of the Polar Bear pins. These proved so popular that at the Foundation's Annual Meeting and Friday Luncheon in Edmonton some two hundred pins were sold (and resold!).

The speaker at the luncheon was Dr. Gareth R. Taylor, Vice Chair of the Awards Committee. His address, entitled "The Hidden Mysteries of Nature and Science - the Importance of Research" was listened to by a large and attentive audience.

John V. Lawer

Following the address a very special presentation was made to David Kruger, 33rd degree Past Grand Secretary General and Past Sovereign Grand Inspector General in Virginia of the Supreme Council A&ASR Southern Jurisdiction, USA, and Honorary Member of the Supreme Council of Canada, in recognition of his continuing supportive leadership roll

In encouraging the establishment of learning centres by The Scottish Rite Charitable Foundation of Canada, Bro. Kruger was presented with the Foundation's first Mentor Bear - a Teddy Bear size bear that will be presented to anyone who donates $1,000 or more to the capital fund for the establishment of learning centres in Canada.

The Luncheon concluded with the grateful receipt of donations from Valleys, individuals and 33rd degree class years for all aspects of the

…continued on back page.

Maternal infection may affect brain development

Can an infection in a pregnant woman cause abnormalities in brain development leading to thinking disorders in a child? That's the intriguing question being looked at by Dr. Albert Wong at Toronto's Centre for Addiction and Mental Health, with new funding from the Scottish Rite Foundation. The answer could shed light on many disparate brain ailments.

Studies done elsewhere have already linked several types of mental disorders with infection endured by a mother during pregnancy. All of them, asserts Dr. Wong, involve some form of cognitive impairment. And since the brain structures necessary for higher thinking are formed during specific critical points in a pregnancy, he is intent on looking closely at the possible connection. "We're going to look at some basic issues at the root at several kinds of cognitive problems," he says. "There is now a lot of evidence developed over the years linking maternal exposure to infectious agents with later neurodevelopmental disorders in the offspring born to these mothers - disorders such as mental retardation, learning disabilities, autism and schizophrenia."

Any infection will do

The really interesting thing is, it does not seem to matter what kind of infection is involved, only that the mother's immune reaction kicks in. "The studies demonstrate a clinically observed association, but it does not look like it's specific to any one infectious agent." Indeed, even a maternal urinary tract infection – a very common occurrence – can increase the risk of mental retardation. "Part of the hypothesis I'm looking at is that it's not the infectious agent, but the maternal immune response to infection that is harmful to the developing brain."

Researchers know the association is there, but they don't know what's going on at the molecular level in the developing brain. Wong intends to look at the molecular basis underlying these established clinical observations. "The idea is to take pregnant rats and expose them to Poly IC, which is a synthetic RNA."

A bit of background: Cells have a nucleus, containing most of their DNA, which is like the software of life. But it's proteins that actually do things; they accomplish specific tasks in the body. DNA codes for the construction of those proteins. To make a protein, a cell's internal machinery copies a section of DNA, which codes for a particular protein, onto a new molecule called messenger-RNA. The mRNA then strings together the proper sequence of amino acids to form the protein.

Wong will inject lab rats with Poly IC, a synthetic form of RNA, because it does not code for any particular protein, yet produces an immune response in the body because it would normally only be found where an infection or damage is present. "The Poly IC tricks the body into believing there is a reason to mount an immune response." Yet because there is in fact no infection, his results will not be clouded by the other effects of a real infection.

"The idea is to give this Poly IC at the time of pregnancy when we know that certain parts of the cortex of the brain are forming." This is something already well understood. The brain forms as a six-layered structure, one layer at a time. It's an ordered sequential process in which each step must be completed in order for the next to properly occur. "We'll give Poly IC just as the first steps in this process are occurring, because we know that in humans exposure at this time is most likely to cause problems later on." Half of the total number of pregnant rats will receive only saline injections, not Poly IC. That's the control group. The lab work then involves killing the baby rats at different times in their development, removing their brains and extracting RNA.

Marvelous micro-arrays

To discover what proteins that RNA was making, Wong will use technological marvels called micro-arrays. These are postage-stamp-sized swatches of material impregnated with DNA in a finely arranged array, with each point on the array a dot of DNA of a particular, known function. His rat RNA is tagged with a chemical label, then washed over the arrays. By looking at where the chemical tag sticks, it becomes clear what that particular sample of RNA coded for, and therefore which proteins were being made, and in what quantities. Comparing these results in the Poly IC rats with the results from rats whose mothers received only saline will show the difference in brain proteins being made in the two groups. This, Wong believes, will be a revealing window into what exactly is happening in developing brains, at the molecular, protein-building level. "Eventually this could have implications for any brain condition that we know is affected by maternal infection."

Not that cures for schizophrenia, mental retardation, autism, and learning disabilities are around the corner. But these methods could reveal new information about the genetics of things like autism and schizophrenia, and possibly lead to new ways to diagnose or screen families for these ailments.

"If we can understand how infection in the mother during pregnancy can interfere with normal brain development, then we would have specific molecular targets to look at. If we know one gene is being expressed too much or that a gene is initiating some kind of biochemical cascade, we might be able to think in term of a drug that could interrupt that cascade."

It's an original line of research – Wong is unaware of anyone else working along similar lines. "So far it has been difficult to get funding for it," he admits. "Research money in Canada is tight, and I'm a junior researcher. So I'd like to thank the Foundation for this. Funding agencies know they take a risk when they fund a junior researcher with a new idea. But if we knew where the findings are going to come from, it wouldn't be research."

2004/05 graduate student awards ($10,000)

New awards

Joyce Clouston-Carlson
Wilfrid Laurier University

Title of Project: *A qualitative study assessing the needs of developmentally disabled aboriginal children and their families*

Brennan Eadie
University of British Columbia

Title of Project: *Attenuating intellectual impairment in Fragile-X syndrome by enhancing neuroplascitity*

Lana Depatie
McGill University

Title of Project: *Executive function deficits in subtypes of Attention Deficit Hyperactivity Disorder: Developmental delay or arrested development?*

Diego Garzon
McMaster University

Title of Project: *Establishing the link: Alzheimer's disease and beta-amyloid deposition and its effects on transcription of brain-derived neurotrophic factor in humans*

Christine Valiquette
Université de Montréal

Title of Project: *Practice and needs analysis aimed at people concerned with using communication aids in mental deficiency*

Renewal of awards for 2nd year

Alan Castel, Ontario
Teena Chase, Nova Scotia
Patrick Malifant, Ontario
Thomas Rhee, Ontario

Renewal of Awards for 3rd year

Dalia Gotlieb-Tanaka, British Columbia
Kyle Whitfield, Ontario

2004/05 college bursary recipients ($2,000)

Meagen Bird, Ontario
Adell Matthys, Manitoba
Shannon Wihlidal, Saskatchewan

Recipients of major grants ($35,000)

Dr. Isabelle Aubert, Sunnybrook Health Centre, Ontario
Dr. Albert Wong, Centre for Addiction & Mental Health, Ontario
Dr. Margaret Fahnestock (renewal for a 2nd term), McMaster University, Ontario
Dr. Jane Rylett, University of Western Ontario
Dr. David Molloy (funded 01-03), McMaster University, Ontario $31,723

Renewal of Grants for 2nd year

Dr. Patrick Cossette, Quebec
Dr. Richard Dyck, Alberta
Dr. Nicolaas Verhoff, Ontario

Renewal of Grants for 3rd year

Dr. Andrea Bernascone, Quebec
Dr. Jessica Ann Brian, Ontario (deferred to 2005)
Dr. Francis Choy, British Columbia
Dr. Christopher Shaw, British Columbia

Is there an insulin connection in the Alzheimer's mystery?

At the Robarts Research Institute in London, Ontario, University of Western Ontario professor Dr. Jane Rylett will use a new Scottish Rite Foundation grant to take a look at yet another aspect of the tangled web involving amyloid protein deposits, dying brain cells, and the mystery of Alzheimer's Disease. She plans to find out more about the interplay between mysterious amyloid protein deposits and the effects of insulin on the brain cells. The insulin connection is not a totally new idea, but has not received much attention. Until now.

Makes sense

Yet it's the kind of connection that makes intuitive sense, even to the layman. Diabetes is a high-profile disease, therefore most people understand that insulin regulates the availability of glucose - blood sugar - to the cells. Glucose carried in the blood is a basic fuel that runs the machinery of the cells, including brain cells. Especially, brain cells, in fact: "Neurons require huge amounts of glucose to function," Rylett points out. "Something like fifty per cent of the glucose that our bodies use, is used in the brain." So if something interferes with insulin, it's logical to expect some consequences involving brain function. And in fact, epidemiologists have noticed a relationship between brain function and insulin.

Epidemiologists concentrate on tracking disease trends and correlations, without looking at the molecular mechanisms involved. The connection they have found is not so clear-cut as a high percentage of diabetes-sufferers among AD victims. But the link between brain function and insulin has caused Dr. Rylett to decide to take a hard look at what insulin might be up to in the brains of AD patients. "One of the enzymes that metabolizes amyloid peptides is Insulin-Degrading Enzyme, or IDE. This enzyme is critical to being able to clear the brain of amyloid peptides," she says.

Which suggests a few interesting possibilities. One is that too much amyloid uses up the available IDE, thus accounting for a buildup of insulin and general disruption of the proper machinery that normally makes glucose available to brain cells. But it's also possible that something is wrong with the IDE itself, leaving the amyloid to accumulate in the absence of the IDE's normal effect.

The situation is complex, but Rylett hopes to find out more about it by taking a fundamental look at brain cells, insulin and amyloid. She will work with cell cultures, those tanks that grow cells for study. She will use neuroblastoma cells, and also neurons derived from rat brains and grown in cell culture (Neuroblastoma cells closely resemble primitive, developing brain cells.) The question is: Does insulin protect these cells from death at the hands of amyloid deposits? Does it help the amyloid to cause cell death? "We're looking at how different insulin concentrations may be neurotoxic or neuroprotective, in the presence of different concentrations of amyloid peptides."

She's particularly interested in the smaller fragments of amyloid proteins which have not yet built up into the large tangles or fibrils that are such a striking feature of microscopic views of Alzheimer's victims' brains. Those small amyloids are the ones that bind to specific sites on the surface of cells, and in doing so may initiate a domino-effect; a chemical pathway that leads to cell death.

Of course, many researchers are looking at amyloid protein deposits, in many different ways. But the role of insulin is not being extensively researched elsewhere. "Amyloid peptides are a fairly hot topic in this field of research," Rylett says. "But to look at insulin and amyloid peptide together is fairly new."

Riddle wrapped in a mystery

Alzheimer's Disease is the proverbial riddle wrapped in a mystery inside an enigma. It begins somehow at the surface of the neuron cell, where the chemical workhorses of life, the proteins, are supposed to bind to sites called receptors, and so begin the normal chemical processes of the brain. Somehow in Alzheimer's, those chemical pathways go horribly wrong. Amyloid is involved, but Rylett's project will take a fundamental look at how it interacts with the insulin that is supposed to be helping feed those glucose-thirsty neurons. "What we will learn from this is what happens beyond the receptor level, when these peptides try to bind to receptors and then either facilitate or inhibit certain processes."

Will this lead to new treatments? Not soon, no. It's the kind of basic research that must be done on the way to inventing new treatments. The idea is to first look at where two adjacent pieces of the puzzle, amyloid and insulin, fit into the larger emerging picture of Alzheimer's. Perhaps it will also help to understand the action of certain drugs even now being used to improve the lot of Alzheimer's victims, although these drugs do not cure the disease.

Rylett says it's gratifying to obtain funding for something that holds great promise that it will eventually fit a new piece into the larger picture this way. She's excited about her work being funded by the Scottish Rite Foundation at a time when research money is tight. "It's hard to get research funding for anything in Canada now."

Better mouse model will lead to better understanding of AD

It's utterly clear under the microscope: The brains of Alzheimer's Disease (AD) patients are a tangle of protein deposits that should not be there: deposits called amyloid and tau proteins, seen in the same regions where brain cells are dysfunctional. But which changes come first? Which are the causes and which are the effects?

To take a better look at these questions, Dr. Isabelle Aubert, Assistant Professor at the University of Toronto and a research scientist at Sunnybrook and Women's College Health Sciences Centre, will look at a newer and better mouse model of Alzheimer's, using new funding from the Scottish Rite Foundation.

Researchers built a better mouse

The new lab mouse is a transgenic type, meaning its genes have been specially modified to include something researchers want to study. In this case, it copies the pathology of AD more closely than was previously possible in a lab mouse. The mouse was developed in the US by a group headed by University of California researcher Dr. Frank LaFerla. When Dr. Aubert heard of it, she established a collaboration with LaFerla's group. Her specialty is the function of the brain's cholinergic system, which is composed of neuron cells producing the chemical acetylcholine to communicate with other brain cells. The cholinergic system is involved in learning and memory, and it is this system which is most disrupted by AD when deposits of amyloid and tau begin to clog the brain and mind.

"There are many mouse models that show over-expression of amyloid, which is one feature of Alzheimer's disease," says Dr. Aubert. "And there are mouse models that show over-expression of tau protein. But this mouse model shows both pathologies, which is much closer to what we see in Alzheimer's disease."

Those pathologies can be seen in the mouse brains when they are examined with a microscope. The question is: what is the connection between these brain changes and the ability of the mouse to learn and remember? "Now we want to see if these mice have the same kind of cholinergic pathology that Alzheimer's patients have – the same loss of learning and memory."

Assessing the cognitive abilities of mice can be tricky. But it can be done because these lab mice are known to be smart, and are capable of what is called 'spatial learning,' such as the ability to negotiate a maze. The degeneration of that learning can become a window into what the degeneration seen in their brains might in fact mean. "With these mice we will look at the cholinergic system," says Aubert. "We will count the number of cholinergic cells and look at their structure to see if the system is impaired."

Bottom line: With this newly funded project, she will in fact be looking at the basic relationships between the amount of amyloid and tau, the degeneration of cholinergic cells, and the learning and memory function seen in the behaviour of these new lab mice. The work will be a combination of microscopic, molecular and biochemical examination of the brain tissue and careful evaluation of the mouse's behaviour.

From there, the question will be: Is it possible to do anything about the brain degeneration and loss of learning ability? "The first part of it is to see if the cholinergic system degenerates," says Aubert. "The second phase is to look at ways to reverse the pathology." The second part of her research will likely involve using chemicals already known to promote cell survival and even neuron cell growth. There are lines of evidence that a natural brain substance called Nerve Growth Factor (NGF) might be able to reverse cholinergic deficits and change the pathology of amyloid and tau protein, which is the cellular signature of AD.

Evidence is not proof

But evidence is not proof. Can NGF promote the survival and growth of cholinergic neurons in a toxic environment composed of both amyloid and tau proteins? Can NGF turn amyloid and tau pathology on and, more importantly – off? Other studies have made the situation seem muddy. Some researchers suspect too much NGF could make amyloid deposits worse. Others found that NGF administration had no impact on amyloid deposits. More recently, researchers suggested that chronic deprivation of NGF can induce amyloid and tau deposits. "So we're left wondering, 'what's the deal here?'" says Aubert. "We want to see if we can regrow these brain cells with NGF and simultaneously monitor the degree of amyloid and tau pathology."

The importance of this question is why researchers the world over are looking at different aspects of it. A clinical test in the US treated eight Alzheimer's patients with genetically-modified cells producing NGF, but they haven't published results yet. Meanwhile, Aubert will get back to basics, using the newer, more accurate transgenic mouse model from California.

Can they expect to clarify the muddied waters? "Because Alzheimer's is such a complicated disease, up to now we've had to use models that looked at only one aspect of it. It's a fair statement to say this mouse model will bring us a step forward to understanding the dynamics of amyloid, tau and the cholinergic system together. Here we can look at a mouse model that shows multiple aspects of the disease." So the research will lead to a greater understanding of the disease mechanisms, which is necessary to design treatment strategies.

…continued from cover.

Foundation's charitable endeavours. A record total of $82,718.95 was received.

The success of the London Centre has been so dramatic, and the need to help dyslexic children so great, that the directors and members at their meetings in Edmonton gave permission to the Valley of Windsor to proceed with their planning to open a Learning Centre in September, 2005, in the Windsor Masonic Temple, following the protocol specified in the Learning Centre's Handbook. Final approval to proceed will be given at the spring meeting of the Directors provided Windsor has the required funding then in place.

A special thank you is extended to Andy Anderson of London who organized the first Polar Bear Classic Walkathon. It was the first of a planned annual series of walkathons to be held on the last Saturday in May to raise capital for the Foundation's Learning Centres program. This year 11 Valleys held walkathons and a total of $34,568 was raised.

In previous years I, and others, have spoken about the need to increase the percentage of our members who donate to the Foundation. It was two years ago that Vice-President Harold Crosby told us that the national participation rate was just 3.2%.Now, as I mentioned at the beginning, the rate has climbed to 6.6%. We are still shy of our minimum goal of a national rate of 10%, but we are trending in the right direction.

A trend that worries me, however, is the declining number of individual donors. In 2003 we had 1,215 individual donors. In 2004, we had 1,125. That is a drop of 90 donors....about 7.5%. I know that our total membership has dropped, and that may explain some of the decline, but this drop in the number of individual donors, if it is a trend, is worrisome.

I realize that some Valleys raise a great deal of money through events, and believe me, we're grateful for their effort and contribution. I certainly understand the concept of value-for-money. I think it's easier to buy a ticket to a golf tournament, and get some tangible benefit for the money, than to make a donation in the Blue Envelope, that does not have a tangible benefit. The simple fact is, we need both. We need individual donations and we need fund raising events. My only concern, as I said earlier, is that the number of individual donors has dropped by 7.5% in the past year.

While we tend to focus on increasing the national participation rate it's important to remember that some Valleys have already exceeded the minimum 10% target.

I'd like to acknowledge the top five Valleys and offer my congratulations on a superb performance. You are an inspiration to everyone.

- Medicine Hat, 25%.
- Central Alberta, 19%
- Sydney, 17%
- Kamloops, 15%
- Victoria, with 12%.

Another way of looking at participation rates is how much the rate has increased over the year. To me, this measurement acknowledges effort. In some cases, the participation rate is sill low, but clearly, an effort is being made to increase the number of donors.

The top five Valleys showing the greatest increase in the participation rate are:

- St. John's, with an increase of 326%. Their participation rate increased from 0.69% to just under 3 per cent. I imagine they'd said it's still low, and it is. But you can't get to 10% if you don't first get to 3 and 5 and 7 per cent.
- Calgary, 209%
- Moncton, 181%
- Campbell River, 180%
- Colville Valley, 117%

I and my fellow Board members believe this issue of participation rate is so vital to our financial health that we will be introducing, for next year's annual meeting, awards that acknowledge the top performers in the two categories I just reviewed: top participation rate and the greatest increase in the participation rate. I hope that the introduction of an awards program will encourage some friendly competition among our Valleys and Valley reps.

I certainly want to thank Don Thornton, Dr. Gareth Taylor, Dr. Paul Fraser and their many colleagues in Canada who adjudicate the applications for grants, awards and bursaries. This is, by no means, an easy task because all the applications have merit. This year, the committee reviewed 78 applications, 33 of which were new applications for major research grants. In all, the committee approved new and renewed major grants, awards to graduate students and bursaries to college student and approved requests worth $491,473.

An initiative of the Foundation to recognizing the effect Alzheimer's can have on family members who must care for loved ones afflicted with the disease was the support given at the suggestion of Director Philippe Decelles to "Baluchon (travel bag) Alzheimer" in Montreal, an organization devoted to giving respite to these care givers. The Foundation received excellent pictorial coverage of our donation in the society's bulletin L'entr' aide-mémoire.

As always, appreciation is extended to the Foundation's representatives in each Valley, the Grand Secretaries and Registrars and the Hamilton office personnel for their commitment to the charity of the Scottish Rite Freemasons of Canada.