

Message from the Scientific Director

Happy New Year, and welcome to this year's first newsletter. Fall was a busy time at INMD. We continued ongoing work with partners and collaborators,



Dr. Diane T. Finegood

and met with our IAB for two days of discussion about the evolution of our strategic initiative.

We were a visible presence at the annual conference of NAASO, the Obesity Society, held in Vancouver. The conference was well-attended, and we enjoyed meeting many people from our research community. Our "speed-networking" event seems to have been a success as many who attended said they really appreciated

the opportunity to meet others from across Canada interested in obesity research.

Our first newsletter this year offers you a variety of news and features, and details about upcoming events. We are pleased to provide you with a profile of the research of Dr. Guang Sun, from Memorial University in Newfoundland. Dr. Sun has identified a new risk factor for insulin resistance and type 2 diabetes. From the other end of the country, we have news from Dr. Jeffrey

Johnson, who spoke to us about some of the results produced by his New Emerging Team, regarding the links between depression and diabetes, and cancer and diabetes.

Also included is an overview of INMD's ongoing collaborations with the Heart and Stroke Foundation of Canada, news about a new intervention strategy website, and general CIHR news. As always, we welcome your feedback.



Website evaluates intervention strategies

To design and utilize effective interventions in public health and health promotion, it is crucial that program and policy decision-makers are able to access and interpret research evidence. To this end, a website has been developed to provide Canadians free access to a comprehensive knowledge translation site.

The project began in 2001 as a CIHR-funded study to elucidate the needs and delivery preferences of decision-makers. Results of the study, headed by Dr. Maureen Dobbins of McMaster University, led to creation of the website. The registry maintained at <http://health-evidence.ca> allows users to sign in, and either browse or search for reliable, up-to-date reviews which evaluate a range of intervention strategies.

Users can browse an area of interest, such as chronic diseases, or mental health, or nutrition. They also have the choice of restricting returns by choosing a number of modifying factors, such as timelines, population characteristics,

type of review, intervention location, and type of strategy.

All reviews have been assessed for methodological quality by two independent reviewers, and a quality rating system is also employed. Creation of a two-page synopsis of each review is underway. The database was compiled through a search of electronic databases, journal table of contents and reference lists.

The website is funded by CIHR, the City of Hamilton's Public Health and Community Services Department, the Education and Development branch of Public Health Research, Institut national de santé publique du Québec, and the Public Health Agency of Canada. It is currently focused on dissemination of information, but the goal is to develop it as a tool to facilitate communication exchange and serve as a networking forum.

CIHR newsletters provide updates on activities and guidelines

CIHR has two new vehicles to communicate with researchers. The first issue of an electronic newsletter for the research community entitled "CIHR – E Alert: News for Researchers" was sent out in October last year. The newsletter includes news about CIHR activities and funding opportunities, and provides links to individual Institute news. The newsletter will be produced on a regular basis, and can be accessed at <http://www.cihr-irsc.gc.ca/e/26626.html>.

Now coming up to its fourth issue is "Ethics Live! @CIHR". This on-line newsmagazine includes articles on a diverse array of topics, such as "New Ethical Requirements at the NIH: Implications for CIHR and Canada", "Draft Guidelines for Health Research Involving Aboriginal Peoples", and "Avoiding Conflicts of Interest". Access to this newsmagazine is at <http://www.cihr-irsc.gc.ca/e/29075.html>.

Diabetics struggle with depression, cancers

Are there links between type 2 diabetes and depression, and type 2 diabetes and cancer? It would be reasonable to guess that living with a chronic disease could lead to depression, but a link to cancer might not be so intuitive.

Dr. Jeffrey Johnson and a team of researchers at the University of Alberta have shown that a link between depression and type 2 diabetes (T2D) does exist, but it is the depression that contributes to earlier onset of T2D in those who are susceptible. They have also confirmed previous data suggesting that living with T2D puts some people at greater risk for cancer-related mortality, and the choice of antidiabetic medications may play a role.

Johnson is Canadian Research Chair in Diabetes Health Outcomes, and Chair of the Alliance for Canadian Health Outcomes Research in Diabetes (ACHORD). ACHORD was funded in 2002 by a Chronic Disease New Emerging Team (NET) grant, offered by a group of stakeholders led by INMD. The NET grant program is designed to develop new competitive research teams, foster multidisciplinary and cross-theme research, train and establish new investigators, and create a team environment that favours the development of new fundable research projects.

The scope of research undertaken by the ACHORD group spans a wide spectrum, but the major focus is on the population health burden of diabetes, particularly as revealed by epidemiological and economic studies. With five primary investigators and more than 25 research associates, trainees and collaborators involved since ACHORD's inception, the range of research topics has become predictably diverse. Johnson explains that depression and cancer were not mentioned in the original grant application.

"In the beginning, they weren't what we described in the NET, but they've

become specific areas of research we've developed since the proposal. The NET has allowed us to expand a lot of our research, and broaden our research interests, and address other important co-morbidities."

Johnson's interest in the link between T2D and depression was sparked by graduate student Lauren Brown, whose clinical experience as a pharmacist had stimulated her interest. Together, they discovered a growing body of literature, but the data was inconclusive and sometimes contradictory. "There were still a lot of questions about the



Dr. Jeffrey Johnson

relationship," explains Johnson. "Everyone seemed to recognize that there was a relationship between depression and diabetes, but nobody had clarified which came first."

Using administrative databases from Saskatchewan Health, and controlling for confounding factors such as co-morbidities, age and sex, the team compared individuals with newly diagnosed T2D to a control group, and found that younger patients with T2D were 23% more likely to have experienced one or more depressive episodes during the years prior to disease onset. Johnson explains, "It is quite likely that depression is

accelerating the onset of diabetes in people who are at risk of developing it."

How does this work? Brown, Johnson and collaborators Dr. Sumit Majumdar and Dr. Stephen Newman suggested in a *Diabetes Care* paper last year that it could be a combination of factors.

"Onset of depression may result in increased weight gain (as a result of the disorder or in relation to antidepressant treatment) and decreased self-care measures such as exercise. Also, people with depression are more likely to abuse alcohol and smoke cigarettes compared with individuals without depression. These behaviors can potentially increase the risk of developing type 2 diabetes." Excessive alcohol use can damage the liver and push glucose production above normal, and smoking damages the vasculature that allows cells to function properly, including in response to glucose and insulin.

What about the other side of the coin? Can T2D cause depression? To answer this, the team did a follow-up survey of individuals from the original database who had shown no evidence of depression. The results, to be published soon, showed that after about five years, people with T2D were no more likely to have developed depression than those without the disease. Johnson notes that these results contradict some previously published studies, and thinks that time may be the salient factor.

"In the longer term, particularly after the onset of diabetic complications, there may be an increased risk of depression."

Although this is logical, one would almost hope he is wrong. People with T2D are already at greater risk for cardiovascular disease, kidney disease and blindness. And, we now know from the ACHORD group that they are also at greater risk of cancer-related mortality. Epidemiological evidence suggested that T2D conferred a greater risk of breast, pancreas, endometrial

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and colorectal cancer. This data, and the enthusiasm of graduate student Samantha Bowker, encouraged Johnson to look deeper.

“This work has spun out of our previous research on drugs used to treat diabetes, and one in particular, metformin,” explains Johnson. “We started to look at metformin and its association with different types of outcomes and mortalities in people with diabetes, and we found that cardiovascular deaths were reduced in people who were using metformin. We had hypothesized this, as metformin has been associated with improving insulin sensitivity.

“We noted, however, that the reductions in all-cause mortality were even greater than the reduction in cardiovascular deaths. We therefore looked at other causes, and noticed that there were differences in cancer deaths. We wanted to look at it more carefully to see if the kind of drugs we use to treat diabetes have any effect on cancer outcome.”

Insulin resistance contributes to the development of T2D. One therapeutic strategy is to provide insulin to the body to overcome the poor response by the cells. Sulfonylurea drugs have the same effect, because they stimulate beta cells to produce more insulin. Another strategy is to make the peripheral cells more sensitive to insulin. Metformin is the most commonly used drug for T2D therapy in Canada, and it works in this way, by increasing the activity of cellular enzymes such as ATPase. The glitazone drug family also increases insulin sensitivity, although through a different mechanism.

The work by Bowker, Johnson, Majumdar and another collaborator, Dr. Paul Veugelers was presented at the meeting of the American Diabetes Association last year. They reported that exposure to insulin or sulfonylureas significantly increased the risk of cancer-related mortality compared to exposure to metformin. This is probably because insulin or insulin-like growth factors are mitogenic and can stimulate proliferation of malignant cells. (This

complication does not apply to people with type 1 diabetes who inject insulin, because insulin does not build to similar levels, and the peripheral cells are still sensitive to insulin.) Full results will be published in *Diabetes Care* this year. But the study did not definitively reveal whether the differing effects of

Johnson is excited about the research capacity of the team. After all, health outcomes can be evaluated across three dimensions he points out - economic, clinical and humanistic.

The co-morbidities related to T2D cut across all three dimensions.



ACHORD Investigators (left to right):
Drs Phillip Jacob, Sumit Majumdar, William Ghali, Ellen Toth and Jeffrey Johnson

the two types of drugs was due to deleterious effect of insulin, or protective effects of metformin, and a more robust study is being designed to address this question. Johnson says they think the evidence points to the former explanation.

“Our hypothesis is that exposure to increasing insulin levels in the face of insulin resistance is not a good therapeutic option as opposed to therapies that improve insulin sensitivity.”

“What we’re trying to do with a lot of the research in terms of diabetes is look at the impact of co-morbidities, of diabetes not just as a chronic disease, but as one of the co-morbidities that affects the population,” he concludes.

“We’re concerned about the interplay of diabetes and other chronic diseases, and the effect on health outcome. All these related conditions - diabetes, mental health, cancer - are huge public issues. Chronic diseases have a huge public impact.”

CIHR wants to help you disseminate your results

INMD is committed to bridging communications gaps between researchers, clinicians, policy-makers and the general public. One of our goals is to make scientific advances accessible to those who do not have expertise in the field, and we are eager to disseminate research information that falls under our mandate to the widest possible audience. To this end, we ask that you contact us if your work has been accepted for publication in a peer-reviewed journal. CIHR is willing to assist researchers in highlighting research findings through the development of communications materials such as news releases, posting of web-based material, and dissemination to various groups through email newsletters. Please contact Nola Erhardt at 604-268-6722 or imnd_communications@sfu.ca.



Obesity epidemic key factor in partnership

The mission of the Heart and Stroke Foundation of Canada (HSFC) is to reduce death and disability from heart disease and stroke. So then why is obesity one of its top strategic priorities?

Being overweight or obese is a leading risk factor for heart disease and stroke. Twenty-six per cent of children and adolescents aged two to 17, and 60 per cent of adults in Canada are overweight or obese. That's why the Foundation is focusing on obesity - through research, advocacy, and health information.

Explains CEO Sally Brown, "If we don't deal with the obesity epidemic, we are taking a step backwards in preventing cardiovascular (CVD)



Finding answers. For life.

disease." In fact, Brown says, that gains resulting from decreased smoking - a "tremendous win" - could be offset by the rise in obesity rates.

HSFC, a not-for-profit foundation supported by more than 130,000 volunteers turns 50 years old next year. Perhaps the wisdom of almost half a century allowed the group to quickly recognize the potential benefits of forming partnerships with CIHR when the Medical Research Council (MRC) was transformed in 2000.

Brown says, "We were really supportive of the transformation. To prepare for it, we took a part of our

research investment and created a strategic envelope of money specifically to partner with the CIHR Institutes."

She says although they initially assumed that most of HSFC's collaborative work would be undertaken with the Institute of Circulatory and Respiratory Health, INMD soon also became a key partner. The Foundation's decision to make obesity a strategic priority meshed perfectly with INMD's decision to focus on this area.

"I have to take my hat off to the leadership provided by Diane Finegood. I think it was very brave of her to choose such a clear and decisive focus for the research that INMD would fund over the next while, because if you make a choice to invest in one area you know you're going to be seen as focusing less on other areas. That's hard. But because of that decision, I think the Institute will have real impact."

The first partnership between HSFC and INMD in 2002 included the Canadian Diabetes Association, The Kidney Foundation of Canada and CIHR's Institute of Circulatory and Respiratory Health. Together these organizations developed a Chronic Disease New Emerging Team grant program, and ultimately funded six research teams over five years.

Two years later, HSFC approached INMD with a proposition to work together to offer personnel awards to build capacity for obesity research. HSFC lead the endeavour - organizing partners, drafting the Request for Applications, and organizing the peer review process. Brown was happy with the outcome.

"We awarded 15 personnel awards collectively through the Target Obesity program. We're very pleased with that."

HSFC and INMD went on to collaborate to support four Obesity

New Emerging Teams through two consecutive competitions and then seven operating grants specific to childhood obesity.



Sally Brown, Chief Executive Officer, Heart & Stroke Foundation of Canada

Grant funding is just one way the two organizations partner. Last October, HSFC and INMD co-sponsored a workshop, along with the Public Health Agency of Canada and the Population and Public Health Institute of the Canadian Institute for Health Information, to identify gaps in obesity policy research, with a focus on the built environment, and economic interventions. The workshop, which brought together researchers, policy makers, the food industry and government officials from all three levels of government, was a huge success.

HSFC and INMD are also working together on an environmental scan of obesity research funding in Canada in order to help the organizations determine how their future funding in the obesity area should best be allocated.

HSFC was the largest funding body

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for CVD research in Canada before CIHR was created and the old MRC budget doubled. Welcoming this growth, the Foundation has not slowed down its own investments and still invests significantly.

“We fund upwards of \$42 million a year in research, so we’re still a large player in health research,” says Brown.

But one change has been HSFC’s funding approach. Although most operating grants in Canada are still allocated to individuals or teams for investigator-driven research - and this remains true at CIHR and HSFC - Brown says HSFC’s research enterprise now includes more strategic research funding targeted at the Foundation’s priority issues.

A newly developed “Managed

Research Cycle” will help to ensure more optimal uptake of research results through a significant focus on knowledge transfer and exchange.

“More and more we need to ensure that the research we fund results in changes to clinical practice or public policy. By fully incorporating potential end users in our Managed Research Cycle which guides our research investments, we help to create synergies among researchers and policy makers that will bring us closer to finding and applying the answers derived from research.”

In addition to its relatively recent focus on obesity, HSFC continues to fund research across the spectrum of cardiovascular and cerebrovascular disease and is developing other exciting partnerships to focus some of its strategic research investments on its

two other mission priorities: stroke and early pre-hospital care (resuscitation) research.

“There’s never an end to the demand for research,” says Brown, “and while the research questions change and we do make progress there is much more evidence needed to help us prevent diseases and increase the quality of care and quality of life that Canadians deserve.

“One thing we’ve learned is the critical importance of getting the evidence right before translating it into changes in care or public policy. Partnerships with agencies like INMD allow us to share knowledge, pool resources, create synergies and take risks. That is what we’re all excited about and why we’re working together. By working together we can achieve more than any one organization could do alone.”

INMD receives accolades for participation in new training program

Scientific Director Dr. Diane Finegood recently accepted an award from the membership of the Kidney Foundation of Canada, acknowledging INMD’s participation in development of the Kidney Research Scientist Core Education and National Training (KRESCENT) program.

KRESCENT is a joint initiative of the Kidney Foundation of Canada, the Canadian Society of Nephrology and CIHR. Flanking Dr. Finegood are (left) Mr. Gavin Turley and (right) Mr. Win Wolfs from the Kidney Foundation of Canada, and (behind) Dr. Kevin Burns of the Canadian Society of Nephrology.



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High serum calcium new risk factor for diabetes

An increase in serum calcium levels causes an increase in insulin resistance, and contributes to the development of type 2 diabetes (T2D), reports a CIHR-funded researcher from Memorial University, Dr. Guang Sun. An increase in serum calcium was also correlated to a decrease in beta cell function.

Sun's study was published late last year in the journal *Diabetes*. This research not only adds to the known list of risk factors for the disease, but because the study subjects were not diabetic, it reveals a molecular change that occurs before clinical diagnosis is possible.

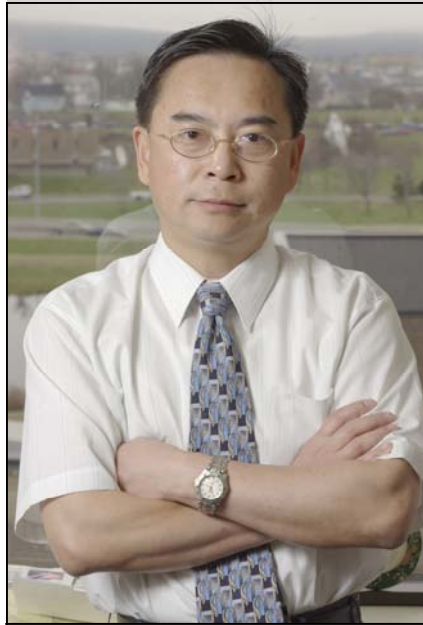
The paper is important, says Sun, because previous studies have always included people with T2D. "This is the first paper to explore the relationship between serum calcium with fasting serum glucose, insulin, insulin resistance and beta cell function in a large population whose blood glucose is under 7 mmol/l." Higher blood glucose constitutes clinical evidence of diabetes.

Sun studied more than 1000 subjects and undertook a thorough examination of possible confounding factors. These included factors that affect serum calcium (other divalent cations, vitamin D and levels of parathyroid hormone), and insulin sensitivity (age, sex, medication status, menopausal status and trunk fat percentage).

He used the homeostasis model assessment (HOMA) for the quantification of insulin resistance, because this method is highly correlated with other measures of insulin resistance in vivo. This careful approach was necessary, he says, because studies in this area have been controversial, even contradictory. The HOMA model can also be used to estimate beta cell function.

Sun's data showed a significant positive correlation between serum calcium with glucose levels and insulin

resistance in both sexes, but data generated by female subjects provided the strongest evidence.



Dr. Guang Sun

Women with the lowest calcium levels had the lowest concentration of glucose and the least insulin resistance, and those with the highest calcium levels had the highest concentration of glucose and the most insulin resistance.

Also, Sun was able to statistically demonstrate an inverse relationship between serum calcium and beta cell function, but only in women.

The reason for the difference probably relates to sample sizes. The study included approximately four times more women than men, so the larger sample size probably allowed the statistical correlation to emerge in

women but not in men.

"We did see the trend in men," says Sun, "but it didn't reach statistical significance."

How does increased serum calcium lead to dysregulation of glucose homeostasis and T2D? Sun points out that insulin secretion from pancreatic beta cells is calcium dependent, and stresses the diagnostic importance of this fact.

"The abnormality reflected by the calcium must come before other clinical symptoms." As well, insulin resistance arises in liver, fat, and particularly muscle cells. So this data is important because "we know that serum calcium plays an important role in cellular functions as a universal messenger. A rise in calcium concentration in the serum can affect cellular functions and lead to abnormalities of metabolism."

In conclusion he says, "We've moved one step forward. We've showed that while calcium level is not the only factor, it is one of the major factors in development of T2D."

Does this mean we need to be careful how much calcium we take in? Not at all. Earlier studies from Sun's lab showed that dietary calcium, even in the form of a supplement, is not significantly correlated with serum calcium levels.

Sun will be continuing his studies in the area of obesity and T2D, using a CIHR-INMD grant to examine gene and mRNA differences in adipose tissue in response to short-term overfeeding in obese and non-obese subjects.

Ethics document being evaluated

The CIHR Ethics Office has announced publication of a CIHR Best Practices for Protecting Privacy in Health Research document, online at <http://www.cihr-irsc.gc.ca/e/29138.html>. During 2005-2007, an Initial Implementation Working Group will promote wide dissemination of the document, particularly among researchers and research ethics boards, and conduct an evaluation of the document's use, usefulness and impact. Compliance with the Privacy Best Practices is voluntary.

INMD FUNDING OPPORTUNITIES:

Research Development and Knowledge Exchange

INMD is committed to funding for workshops, consensus conferences, meetings to stimulate research collaboration and similar activities under a Request for Applications (RFA) for Workshop Support – Research Development and Knowledge Exchange. This RFA is open to all researchers working in any area within the INMD mandate. However, eligibility requirements specific to this RFA include: the meetings funded must be held for a limited number of persons who have been individually invited to attend; workshops must be a meeting of a limited number of persons individually invited to address specific questions or problems; and funding may not be used to support congresses, annual meetings, or conferences although it may be applied to gatherings that meet the above criteria and are being held within a larger congress or conference. As much as \$15,000 is available per annum, although there is no restriction on the size of the proposed activity budget and applicants are encouraged to apply for additional contributions from other institutes and funding sources. For more information about the timelines consult <http://www.cihr-irsc.gc.ca/e/26887.html>. For questions about this initiative and research objectives contact:

Paul Belanger, Assistant Director - Ottawa
Tel: (613) 941-6465; E-mail: pbelanger@cihr-irsc.gc.ca

Obesity Grants

INMD has issued a priority announcement for operating grants under the initiative Excellence Innovation Advancement in the Study of Obesity. Priority announcements fund highly rated research applications that are determined to be relevant to specific CIHR research priority areas and do not receive funding through CIHR's regular competitions. The deadline for the applications is the same as the deadline for the CIHR open operating competition due March 1, 2006. For more information check the INMD funding page at <http://www.cihr-irsc.gc.ca/e/26887.html>. For questions about the objectives and relevant research areas, contact:

Paul Bélanger, Assistant Director - Ottawa
Tel: (613) 941-6465; Email: pbelanger@cihr-irsc.gc.ca

Diabetes Surveillance

INMD, in partnership with Health Canada and the Public Health Agency of Canada, is requesting applications for operating grants under a Diabetes Surveillance System initiative. Registration deadline is May 1, 2006. The objectives of this initiative are to enhance understanding of the impact of diabetes on the health care system and on the health of Canadians, and to encourage linkage and/or comparison of the National Diabetes Surveillance System (NDSS) data with clinical, other administrative or survey data. A portion of the funding will be targeted for projects that focus on the prevalence and incidence of diabetes and its complications in Aboriginal Canadians. For questions about this initiative and research objectives contact:

Hasan Hutchinson, Assistant Director - Burnaby
Tel: (604) 268-6706; E-mail: hasan_hutchinson@sfu.ca

Travel Funding

INMD has launched a new funding initiative for post-doctoral fellows, new investigators, and doctoral students. This initiative will provide funding for travel to conferences, symposia and workshops to present research. Application deadlines will be in February. More information can be found on the CIHR website at:

<http://www.cihr-irsc.gc.ca/e/12043.html>, or contact Charlene Phung at inmd_projects@sfu.ca.

Visit our website at <http://www.cihr-irsc.gc.ca/e/13521.html> for updates on funding opportunities.

MEETINGS AND CONFERENCES:

**National Council on Ethics in Human Research National Conference:
Creating and Maintaining Trust - Ethical Issues in Research with Humans**
Ottawa, ON

Feb. 18-29, 2006
<http://www.ncehr-cnerh.org>

Experimental Biology: Advancing the Biomedical Frontier
San Francisco, CA

April 1-5, 2006
<http://www.faseb.org/meetings/eb2006>

**12th International Qualitative Health Research Conference:
Understanding Differing Perspectives in Health and Health Care**
Edmonton, AB

April 2 - 5, 2006
<http://www.uofaweb.ualberta.ca/iiqm/QHR2006.cfm>

**The Canadian Public Health Association's 97th Annual Conference:
What Determines Public Health?**
Vancouver, BC

May 28-31, 2006
<http://www.cpha.ca/>

Visit our website at <http://www.cihr-irsc.gc.ca/e/13521.html> for constantly changing information about conferences and meetings.

