

HEALTHY INVESTMENT

Photography: Marianne Helm



Drs. Marissa Becker, Bob Schroth, Shyamala Dakshinamurti and Rakesh Arora have all received awards from the Manitoba Research Council and the Manitoba Medical Services Foundation to carry out research in their respective fields.

MANITOBA AGENCIES TEAM UP TO PROVIDE MAJOR FINANCIAL SUPPORT FOR HEALTH RESEARCH PROJECTS



One is a doctor who works in the intensive care unit at Children's Hospital. Another is a dentist who spends a portion of his time at a clinic teaching kids about the benefits of oral health.

A third is a clinician who works in the HIV Clinic at the Health Sciences Centre, while a fourth is a cardiac surgeon who co-founded a national organization to help heart patients.

All four of these individuals may work in different areas of the health-care system. But they all have one thing in common: a desire to improve the delivery of care for Manitobans. That is one reason why they have each received clinical research professorships through a special partnership between the Manitoba Medical Service Foundation and the Manitoba Health Research Council. The awards are in the form of three-year research grants totalling \$170,000.

"The intention is to free up these clinicians so they can do research," says Dr. Greg Hammond, Executive Director of the MMSF. The award buys time for clinician-researchers to step away from clinical work in order to focus on an important scientific question.

Typically, recipients of the MHRC/MMSF awards are in their first seven years of their careers and have established their own research specialties, says Hammond, noting that receiving such an award at that time can be particularly valuable. Many recipients of the MHRC/MMSF awards have built on their discoveries and followed up with prestigious national research awards. "We've been told that these grants have given their careers a real boost," says Hammond, noting that having such a research funding program available helps Manitoba compete for talented and innovative scientists.

The awards are designated as F.W. DuVal Clinical Research Professorships, named for a long-time member of the MMSF board, and John Henson Clinical Research Professorships in Population Medicine, named for a former vice-president of Manitoba Blue Cross.

A wide range of specialists have received the awards over the years and have used their time to investigate many different medical questions. Having the award for population medicine available also supports research related to disease prevention and the determinants of

health. "Quite often a clinician will become interested not only in their own patient but by the population that patient represents," notes Hammond, who says that Manitoba is an excellent place to do population health research.

The awards provide a benefit to the University of Manitoba, where recipients teach the next generation of health-care providers, and to Manitoba's hospitals and their patients, which benefit from new approaches and greater expertise. "A lot of their excellent researchers are also excellent clinicians. Sometimes they're unique because they have a special niche," he says.

The MMSF has its roots in Manitoba Medical Service, a not-for-profit entity founded in the 1940s to make health insurance available to Manitobans. In time, the insurance functions of the MMS were overtaken by the development of universal public health in Canada and the establishment of Manitoba Blue Cross for insurance of health services not covered by medicare.

When MMS was dissolved in the 1970s, its remaining funds – totalling \$455,697 – were used to establish a foundation to support medical research and education in Manitoba. "The MMSF portfolio has grown to be approximately \$8.4 million," says Hammond. "Manitoba Blue Cross continues to play an important role, providing sound business advice, capital contributions, research funding and administrative costs."

The Manitoba Health Research Council – a provincially funded agency with a mandate to support basic, clinical and applied health research – joined forces with the MMSF in 2009. Christina Weise, Executive Director of the MHRC, says the partnership has allowed for the expansion of the clinical research professorship program. "Thanks to this partnership, we have been able to increase the number and breadth of clinician scientists doing important medical research in Manitoba," says Weise. This special report, sponsored by the Manitoba Health Research Council, highlights the work being done by four MHRC/MMSF clinical professorship recipients.



BLUE BABIES

Researcher tackles pulmonary hypertension in newborns



Not every birth ends with that magical moment when the baby begins breathing, loses its blue sheen and turns a healthy pink.

In some cases, a newborn will suffer pulmonary hypertension, a potentially fatal condition that makes it difficult for the baby to breathe. Dr. Shyamala Dakshinamurti wants to know why some newborns experience this problem – and what can be done to prevent it. Since 2010, the Manitoba Medical Services Foundation and the Manitoba Health Research Council have been supporting her efforts to find out.

Pulmonary hypertension occurs as a result of difficulties in delivery, such as compression of the umbilical cord or a bowel movement at birth, which results in the tarry meconium (the substance voided from the bowels before the baby begins feeding) getting into the airway. When this happens, the newborn is unable to get enough oxygen.

Although only one to six babies per 1,000 have hypertension, they make up 10 per cent of babies in the Neonatal Intensive Care Unit at Children's Hospital, she says. "These are the sickest babies in the NICU," says Dakshinamurti, a member of the Pediatrics and Physiology Departments at the University of Manitoba's Faculty of Medicine and the Biology of Breathing Group.

Dakshinamurti, who does clinical work on call at the Children's Hospital NICU, notes that the body goes through a remarkable change at birth, and the babies she's focusing on are those who need extra help through this transition. "It's something we take for granted: that when the baby takes its first breath the heart will direct blood to the lungs," she says. "At that moment, you go through the transition from oxygen coming from the placenta to oxygen coming from the lungs. You go from five per cent of cardiac output going to the lungs to 100 per cent."

Pulmonary hypertension causes the vessels in the lungs to go into spasm, making it difficult for the heart to pump enough blood through them, raising the blood pressure and reducing the amount of oxygen to the baby's cells. "The heart's not used to pumping against resistance, so it's under a lot of strain," she says, noting that the condition can lead to heart failure.

In her research, she's examining the mechanisms that allow blood to circulate to the lungs for oxygenation, focusing on the agents Thromboxane and Prostacyclin. Cells produce Thromboxane in response to injuries, causing inflammation. Before birth, when the baby is not breathing and is getting oxygen from the placenta, Thromboxane keeps the heart from pumping blood to the non-working lungs. But after birth, Thromboxane levels should go down and Prostacyclin levels should go up, opening up the blood vessels and allowing blood to flow to the lungs.

Treating the condition with these agents is no simple matter. Eliminating Thromboxane isn't an option because it is needed for blood clotting. Giving the baby Prostacyclin is a challenge because it lowers blood pressure everywhere in the body. Using animal and cell-culture models, she's also researching the role of a molecule called Cyclic AMP, which signals to the body's cells to make the heart muscles contract and blood vessels to the lungs dilate.

Dakshinamurti says her objective is to improve treatment for pulmonary hypertension using drugs that are already part of pediatric practice, rather than to search for a "silver bullet" that would take many years to be developed. One of the treatments is a cardiac drug called Milrinone, which helps the heart to pump and also helps to make sure that the natural Prostacyclin the baby needs to keep blood vessels in the lungs open is used effectively. Milrinone prevents the breakdown of Cyclic AMP, the molecule Dakshinamurti is researching in the lab, she says.

Could something as simple as giving pregnant women a dose of Vitamin D during a regular medical check-up effectively ensure healthier babies at birth?

That's the main question Dr. Bob Schroth intends to answer in a research project he is currently conducting with support from the Manitoba Medical Services Foundation and the Manitoba Health Research Council.

The health benefits of prenatal Vitamin D are becoming clearer all the time, and the question now is how best to ensure that all pregnant women have enough to give their babies a good start in life. Schroth's research will determine whether giving pregnant women high doses of Vitamin D during visits to their physicians is an effective way to proceed.

The project flows from the report of the Maternal and Child Healthcare Strategy Task Force in 2007, which recommended giving pregnant women 100,000 IU of Vitamin D during pregnancy.

Vitamin D is increasingly seen as essential to many aspects of health in childhood and throughout the lifespan, including stronger bones, better balance, less depression and better oral health. Supplementation is especially important for Canadians, says Schroth. "We live in a northern environment where for six months of the year the angle of the sun doesn't allow us to get Vitamin D from sunlight," he says.

More than 280 women have been recruited for the project, says Schroth, a professor in the Department of Pediatrics and Child Health at the University of Manitoba's Faculty of Medicine, and a member of the Department of Preventative Dental Sciences in the Faculty of Dentistry.

Recruited from women presenting to the Outpatient Department at the Women's Hospital, the women are being divided into a test group and a control group. Members of the test group will be given two 50,000 IU doses of Vitamin D – one each in the second and third trimester – in addition to their usual advice to take a prenatal multivitamin (containing Vitamin D) and practise healthy eating. Members of the control group will receive the same prenatal care, dietary and multivitamin advice, but won't receive the two extra high dosages of the vitamin.

At birth, the Vitamin D levels in umbilical cord blood will be examined to measure the effect of the supplementation. The babies will then be examined at one year old to assess dental health and overall health and development.

The idea behind the two high-dose supplements, notes Schroth, is rooted in the understanding that not all mothers-to-be have equal access to a healthy diet. As well, some women who experience pregnancy-related nausea may find it difficult to take a vitamin at times, and all people are prone to forgetting a vitamin now and again. "Even me," he notes. "I keep the Vitamin D right beside my toothbrush so I'll see it, but I sometimes forget."

Preliminary data are encouraging. Babies whose mothers were given the supplement were nearly twice as likely to reach the Vitamin D target of 75 nmol per litre. Overall, the mean Vitamin D level for the supplement group was higher than for the control group, although still below the 75 nmol per litre level. "It's a modest increase in the cord Vitamin D levels at birth," says Schroth. High-dose supplementation is not intended to replace multivitamins and healthy nutrition, notes Schroth. "This is one layer added to prenatal care," he says.

The project is a team effort with Dr. Cheryl Rockman-Greenberg, Head of Pediatrics and Child Health for the Winnipeg Health Region, Dr. Margaret Morris, Head of the Department of Obstetrics and Gynecology at the University of Manitoba's Faculty of Medicine, and Pat Gregory, Director of the Women's Health Program for the Winnipeg Health Region.

The research award from the foundation allows Schroth to take time away from his work at the Mount Carmel Clinic and the Winnipeg Health Region's Access Centre at 640 Main Street. His clinical and research work are both aimed at improving dental health among at-risk populations, and he notes that an early start is needed to achieve that. "Often, we only start to look at dental issues once the teeth are there," he says. "Maybe pregnancy is the time. The teeth are starting to calcify in the second trimester. It's the perfect window to make sure that the building blocks are there for dental health."

A HEALTHY START

A prenatal dose of Vitamin D may enhance infant health



QUICK RESPONSE

Improving infectious
disease treatment in
vulnerable populations



The same vulnerable population that is most likely to use hospital Emergency Departments as their primary health-care setting is also at a higher risk for HIV.

With that in mind, Dr. Marissa Becker, Associate Director of the Manitoba HIV Program at Health Sciences Centre and a member of the University of Manitoba's Centre for Global Public Health, is studying the effectiveness of providing rapid HIV testing in the Emergency Department.

Becker is going into the final year of an award from the Manitoba Health Research Council and the Manitoba Medical Services Foundation to support her research on HIV prevention and care in Winnipeg and in India. "The best way to treat HIV is to get people into treatment early," says Becker. "It's significant from an individual perspective and from a public health perspective."

During the course of the study, all adults presenting to the Emergency Department at Health Sciences Centre were eligible to participate. More than 500 consented to a finger-prick HIV test. The advantage of testing in Emergency is that it provides an instant answer rather than the longer wait needed for traditional lab tests. And offering the test in Emergency reaches people who don't have a family doctor or see a doctor for a regular check-up.

This study demonstrated a high detection rate of new HIV cases indicating that the Emergency Department at HSC may be a good place to utilize this type of test. Also of importance from this study was the demonstration of very timely linkage to care – all patients newly diagnosed with HIV were seen by a member of the Manitoba HIV Program within 48 hours.

"People are coming in for HIV treatment quite late in their disease course," she says, and this puts both themselves and their partners at greater risk. "Without knowledge of one's status, an undiagnosed individual may not take the steps to protect their partners from further transmission."

Becker is also working on the education, prevention and care of HIV among vulnerable populations in Karnataka, India, where she spent three years earlier in her research career. In Karnataka, she has been working with sex workers, particularly those new to sex work, and examining their access to health care, services, and HIV prevention information.

During the research in India, 1,500 female sex workers were given a questionnaire and interviewed, especially regarding key transition events in their lives, such as when they first began sex work. "A lot of what we think is happening is that the risk period is early in her transition to sex work," says Becker. "Awareness isn't there around condom use, care centres, education."

Though southern India and Winnipeg may seem a world apart, Becker is interested in how understanding principles around prevention and care in one setting can help in another. "One of the things I've always been interested in is to link up the work I do in India with the work I do in Canada."

Next year she intends to do a study of "missed opportunities" to diagnose patients with HIV. Working with patients who have recently tested positive for HIV, she intends to use the Manitoba Health database to determine if they had earlier presented with infections such as TB that could be markers for HIV. The research was inspired by a patient who had several visits to health-care professionals with conditions that suggested he had HIV over a six to 12-month period before being tested.

Her award from the MHRC and the MMSF frees Becker from some of her clinical work at the Manitoba HIV Program at HSC and at the Nine Circles community health centre. At the same time, working with patients inspires her research. "I love the combination of the two because the clinical work allows me to think about my research in another way and the research informs my clinical work."

Waking up after an operation can be disorienting. But some patients experience a more severe form of post-op confusion known as delirium – a condition that can seriously hamper their ability to recover from surgery.

Dr. Rakesh Arora, Medical Co-Director of the Intensive Care Cardiac Surgery Unit at St. Boniface Hospital, is leading an effort to better predict and prevent delirium in cardiac surgery patients. A recent recipient of the MHRC/MMSF Dr. F.W. DuVal Clinical Research Professorship, Arora will use the award to head a national effort to identify and reduce post-op delirium.

With a background that includes both cardiac surgery and intensive care, Arora's focus is "how to optimize patient care" so that a patient's health is supported not just by the cardiac surgery, but by the entire pre- and post-operative experience. This is where the research into delirium comes into play.

Health professionals have long been aware of the phenomenon, but have only more recently seen it as a significant factor affecting patient outcomes following heart surgery. "In the past we called it 'pump-brain' after being on the heart-lung machine and thought it was a transient and unimportant complication," he says. "But that's not the case. It's associated with a number of bad outcomes, including increased length of stay in hospital, decreased independence and increased rates of death."

While many patients experience some confusion upon waking up from their anesthetic, delirium is a more serious form of brain dysfunction that typically occurs one to five days following surgery. One of the challenges in developing treatment strategies for this problem is that delirium itself isn't always obvious. While some patients have "excited delirium" and become quite agitated or disruptive, many others experience a "quiet" delirium. "These patients appear very sleepy or unresponsive and this form of delirium often goes undetected but carries at least an equal risk of bad outcome as those who experience the agitated delirium," says Arora.

As a result there is lack of understanding of how common delirium actually is in patients undergoing heart surgery, with estimates ranging from three per cent to 70 per cent. A further challenge in delirium is that a problem in the brain can not yet be determined by a blood test, the way liver or kidney problems can be. The first step, says Arora, is to implement a standardized way of screening patients at the bedside for delirium following a heart operation. "By doing this we can not only know how common the problem is, but also determine which patients are at highest risk for developing delirium."

Since 2010, the cardiac surgery health-care teams have supported the effort to assess patients and learn more about delirium, he says, adding, "This program's success will be due to, in no small part, our teams' buy-in to make this happen."

Arora will begin his research by using information gathered in the cardiac surgery intensive care unit and post-surgery in-patient ward since 2010, when nurses began using the Confusion Assessment Method (CAM) – a technique for identifying delirium. "Since implementing a formal delirium screening program, we have determined that approximately one in five patients suffer from delirium following their heart operation." Arora plans to investigate the differences between patients who were deemed to be delirious by the CAM assessment and those who were not. With this information he plans to create a easy to use "score card" so that physicians can clearly identify which patients are most at risk for delirium, before their operation, and then "tailor" their hospital and surgical care to hopefully prevent this potentially life-threatening complication from occurring.

The Cardiac Sciences Program at St. Boniface Hospital will be the pilot site for research by colleagues across Canada who are connected through the Canadian Critical Care Cardiovascular Society (CANCARE Society: www.cancaresociety.com), which Arora founded and currently chairs. In addition to developing a national standard delirium screening program for heart surgery patients, Arora is also investigating whether the condition can be triggered by environmental factors, such as noise in a patient's room.

HEART TO HEART

Study seeks to learn more about delirium in cardiac patients

