Medical Research Council of Canada

A Legacy of Excellence

1960-2000

40 years

MRC CRM

Medical Research Council of Canada
Conseil de recherches médicales du Canada

Canada

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Message from the President

Henry Friesen, M.D.

OVER THE PAST 40 YEARS, WOMEN AND MEN STRIVING TO REACH THE PINNACLE OF EXCELLENCE IN HEALTH RESEARCH HAVE BEEN SUPPORTED IN THEIR EFFORTS BY THE MEDICAL RESEARCH COUNCIL OF CANADA. INDEED, THE MRC HAS BEEN AN INTEGRAL PART OF MY OWN CAREER. THE RESEARCH ADVANCES I HAVE MADE, BEGINNING WITH THE DISCOVERY OF PROLACTIN, WOULD NOT HAVE BEEN POSSIBLE WITHOUT ITS SUPPORT. THANKS TO THAT SUPPORT, MANY THOUSANDS OF COUPLES TODAY KNOW THE JOYS OF PARENTHOOD WHO OTHERWISE MAY NOT HAVE — JUST ONE OF THE MANY EXAMPLES OF THE DIRECT BENEFICIAL IMPACT MEDICAL RESEARCH HAS HAD ON THE LIVES OF INDIVIDUALS.

Over the past decade, I have had the opportunity, and the privilege, to return the favour. I have been able to assist in ensuring that researchers continue to receive the same support I was so fortunate to have, and to head an organization which every day is devoted to making a difference in the lives of Canadians.

To succeed, a research enterprise must always be looking to the future — to the next discovery, but even more importantly, to the next generation of health researchers. Without the initial harnessing of talent, there would be no health research enterprise in Canada. MRC has been proud of the central role it has played in harnessing the talent of Canada's health researchers. Today, many deans of research at Canada's medical schools and heads of major departments in the health sciences are MRC alumni, doing their part in turn to continue the cycle of innovation.

This publication is not about an organization. It is about people — the people whose work has given Canada a well-deserved reputation for excellence in health research throughout the world, who make us confident in our health care system, and whose efforts the MRC has supported over its lifetime.

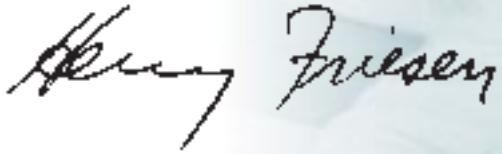
The first two chapters provide a historical overview of the past 40 years. The next two chapters examine some of the innovations that have characterized MRC's work in the 1990s. Finally, we look to the future — to the health researchers whose work is making a difference and to the new world of the Canadian Institutes of Health Research (CIHR).

Today, the CIHR is well underway. But our job is not done. As we look ahead, I encourage all members of the health research community to continue to work to achieve the next goal, that of ensuring that the federal government invests one per cent of all health care costs in health research. Through CIHR, through the Canada Research Chairs, and through leveraged funding from partners, we should continue to strive towards an annual investment of $1 billion for health research by the federal government. This total will position Canada as an internationally competitive funder, allowing us to excel in the global arena.

It is not often that an organization asks to be disbanded. But that is exactly what the Council of the MRC requested of the federal government. We asked, because we knew that it was time to implement a new vision of health research for the 21st century, and we knew that the best way to do that was through thematically linked institutes creating virtual networks of researchers coast to coast — the CIHR structure.

But as we leave, it is important that we pause to celebrate the solid legacy of excellence in health research that was the hallmark of the MRC throughout its existence. It is that legacy we celebrate in this publication.

That legacy would not be possible without the people who are responsible for MRC's successes — my predecessors as president of MRC; the men and women who have served as Council members over the years; the many hundreds of researchers who have taken time from their own work to act as MRC regional directors, peer reviewers, and members of standing committees; and last, but by no means least, the dedicated staff of MRC who have worked for its success for so many years. I thank them all.



Henry Friesen
President, Medical Research Council of Canada
1991 - 2000

Chapter 1:
A Long and Distinguished History

When Frederick Banting, Charles Best, J.J.R. MacLeod, and J.B. Collip produced the research that led to the discovery of insulin in 1921, their achievement created new hope for people with diabetes. But the reverberations of their discovery extended far beyond the confines of one disease. That these young, relatively inexperienced researchers could break open this major research problem, providing hope and life for sufferers of this lethal disease affecting millions, caught the imagination of people around the world, and demonstrated that Canada had world-class researchers whose efforts deserved to be supported. Their discovery led, indirectly, to the creation of the Medical Research Council of Canada.

Did you know...

In 1921, in the time of Banting and Best, 1,100 women died in childbirth in Canada. In 1994, only 10 women died in childbirth across the entire country. Medical research has changed maternity from a life-threatening into a life-enhancing experience.

These eminent scientists believed that government should have a role in funding medical research in Canada, just as it funded other types of scientific research. In 1936, thanks to the perseverance of Dr. Banting, the National Research Council of Canada (NRC) established the Associate Committee on Medical Research. Its initial budget was $53,000. Dr. Banting was the first chair of this committee, whose membership was largely composed of representatives of the nation's medical schools. One of its first decisions was to not establish central laboratories for medical research, but rather to support research in the universities. To that point, outside of the University of Toronto and McGill University, faculty with an interest in research had little or no institutional support. This decision has had a central influence on the subsequent development of medical research in Canada.

In 1946, the Associate Committee was replaced by the NRC Division of Medical Research. The discoverers of insulin continued to play a central role in promoting medical research in Canada, as J.B. Collip headed the division. Like its predecessor, the Division of Medical Research had no laboratories of its own, and focused its activities on supporting extramural research in universities. The Division's initial budget of $200,000 had grown to some $900,000 by 1957, and research supported by the Division resulted in 950 publications in the period 1956-59 alone.

Early Canadian Research Achievements

- In the late 1930s, **W.E. Brown**, of the University of Toronto, demonstrated the value of bromide and ethyl chloride as anaesthetics.
- During the 1930s and 1940s, **Wilder Penfield** developed a brain-mapping technique that paved the way for modern neurology and the treatment of diseases affecting the central nervous system. Penfield later developed a surgical method for treating epilepsy that became known around the world as the "Montreal method."
- In the early 1950s, the **Connaught Laboratories** at the University of Toronto played an essential role in developing a polio vaccine to combat a poliomyelitis epidemic that threatened thousands of Canadians.

"The most commonly expressed desires were for some form of senior research appointment tenable in the universities, for some assurance of continuity of support for research, and greater freedom in the administration of grants."

Results of a survey of research programs and needs of medical schools in Canada conducted by Dr. Frederick Banting and Dr. Chester B. Stewart (1946), reported in *Proceedings of the First Meeting*, Medical Research Council, March 8-10, 1961.

In 1960, the Medical Research Council was established as an autonomous body within the administrative framework of the NRC. The new body had an initial budget of $2.3 million, its own administrative structure, and the freedom to develop its own policies. The new MRC focused its initial efforts on strengthening medical research in universities through a series of programs designed to aid researchers, from undergraduate students to the most senior researchers. By providing ongoing support in this manner, MRC helped to build local research capacity while underscoring the importance of having faculty members devoted full-time to research and of providing training opportunities, not only in clinical practice but also in research. In 1963, MRC established a scholarship program to provide talented young researchers with the means to conduct independent research after completing their formal training.

The decade between 1960 and 1970 was a period of exponential growth for medical research in Canada. The MRC budget increased 15-fold. The number of schools of medicine grew from 12 to 16, and MRC began accepting applications for research funding from Canada's 10 schools of dentistry, eight schools of pharmacy, and school of veterinary medicine.

In 1969, Parliament passed the *Medical Research Council of Canada Act*, which formally created the MRC as an autonomous crown corporation, reporting to Parliament through the Minister of National Health and Welfare, and ending MRC's 32-year relationship with the NRC. Its mandate was "to promote, assist, and undertake basic, applied and clinical research in Canada in the health sciences; and advise the Minister of Health in respect of matters relating to such research."

Over the subsequent 30 years, under the guidance of its five presidents and two acting presidents, the MRC has continued to expand the boundaries of health research.

The 1970s: A period of growth

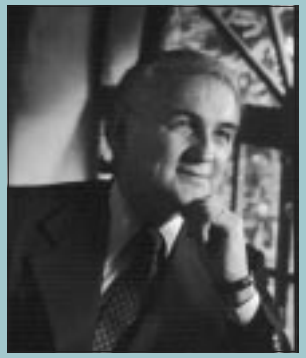
In its first year of existence as a crown corporation, the MRC received $27.2 million, which funded some 1,200 researchers. By the mid 1970s, its budget had increased to $47 million and the number of supported researchers to more than 1,500.

MRC Presidents

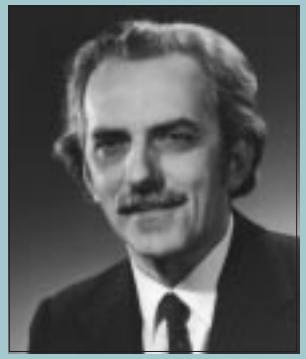
1960-65: Ray Farquharson, M.B.E., M.B., F.R.C.P.(C), F.R.C.P., M.D.(Hon.), D.Sc.(Hon), F.A.C.P., F.R.S.C.

1965-77: G. Malcolm Brown, M.D., C.M., D.Phil., LL.D., D.Sc., M.D.(Hon), F.R.S.C., F.R.C.P., F.R.C.P.(C), F.A.C.P.

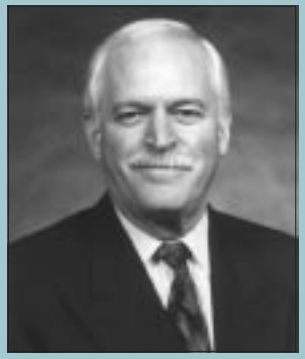
1977-78: Jean de Margerie, M.D., D.Phil., F.R.C.S.(C), F.A.C.S. (acting)



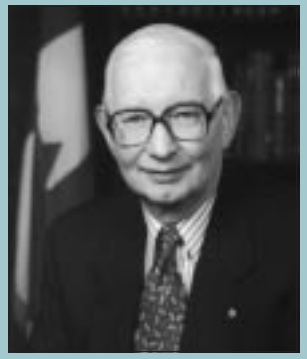
1978-81: René Simard, M.D., D.Sc., F.R.C.P.(C)



1981-91: Pierre Bois, M.D., Ph.D., F.R.C.P.(C), F.R.S.C.



1991: David Hawkins, M.D., F.R.C.P.(C) (acting)



1991-2000: Henry Friesen, O.C., M.D., F.R.C.P.(C), F.R.S.C.

The 1960s and 1970s

- **Bruce Chown**, a pathologist at the Winnipeg Children's Hospital, devoted his career to understanding and treating erythroblastosis fetalis, or Rh disease, caused by a fetal blood factor commonly known as the Rh factor. He subsequently set up the Rh Laboratory to manufacture Rh immune serum under license in 1968. Thanks to his work, the vast majority of potential Rh disease in Canada and around the world has been eliminated.

- In 1960, at the Hospital for Sick Children in Toronto, orthopaedic surgeon **Robert Salter** developed the "Salter Operation" for hip dislocation in children. The procedure is still used worldwide. In the 1970s, Dr. Salter recognized the therapeutic effectiveness of continuous passive motion (CPM) to the repair of cartilage injuries, a finding that has been translated into clinical application throughout the world. By 1998, CPM had helped more than five million people, and offers potential for helping millions more.

- The survival rate of newborns, especially premature infants, suffering from acute respiratory distress rose from 25 per cent to 75 per cent at Winnipeg's Children's Hospital, after **Victor Chernick**, of the University of Manitoba, decided to approach the problem in a new way. Rather than applying increased air pressure to the baby's lungs and airways, he surrounded the baby's chest wall with a constant negative pressure, assisting the air flow in and out of the lungs while avoiding the dangers of an indwelling tube in the infant's windpipe or of applying increased pressure to the lung tissues.

Important new initiatives in the 1970s included support for clinical trials in perinatology and the establishment of MRC Groups and program grants to promote multidisciplinary research. In 1971, MRC established a clinical trials grant committee to support research into the potential benefits and drawbacks of new diagnostic and treatment protocols.

A Commitment to Ethics

Throughout its existence, the MRC has broken new ground in many different areas, including taking a leadership role in the area of ethics.

In 1962, MRC asked the National Research Council to join it in reviewing the use of animals in research. This led to the establishment of the Canadian Council on Animal Care in 1968.

In 1976, the MRC established a Working Group on Human Experimentation. Based on its work, MRC subsequently developed and published guidelines on the ethics of research involving human subjects. It also provided leadership in developing a Canadian vision of the ethics of genetic engineering.

In 1989, MRC spearheaded the foundation of the National Council on Ethics in Human Research (NCEHR), to which it provides funding, along with the other granting councils, Health Canada, and the Royal College of Physicians and Surgeons. NCEHR carries out education and awareness activities to help Research Ethics Boards to implement ethics policies.

In the 1990s, MRC undertook a review of existing guidelines on ethics, in consultation with the Social Sciences and Humanities Research Council of Canada (SSHRC) and the Natural Sciences and Engineering Research Council of Canada (NSERC). A task force composed of representatives of all three councils consulted with researchers across Canada to develop a common approach to ethics across traditional disciplinary boundaries.

In September 1998, the three councils published *The Tri-Council Policy Statement on Ethical Conduct for Research Involving Humans,* the first such initiative in the world. Institutions and researchers must now comply with that policy statement in order to receive funding or support from any of the three federal granting councils.

Medal commemorating the MRC's 25th anniversary celebrations.

The 1980s: Broadening the mandate

The 1980s saw the development of MRC's first five-year plan, which provided a new focus for MRC's work. By the end of the 1980s, the Council's budget had nearly tripled, from $70 million to $202 million. New programs were being developed, including the MRC Scientist program and a new biotechnology training program. This last was seen as holding great promise for improving the diagnosis and treatment of disease.

The late 1980s was also a period of growing awareness of the importance of science and technology to a healthy economy. Governments began to develop new ways to work with the private sector and industry. The University–Industry Program, developed in 1987, provided a means of linking university research with industry, increasing the likelihood that the economic benefits of research funding would be realized in Canada.

The third theme that characterized the 1980s was a trend toward greater support of multidisciplinary research. Program grants began to support an increasing number of research teams, as well as individual researchers.

Research achievements of the 1980s

- **Albert Aguayo** proved the seemingly impossible by regenerating and regrowing damaged spinal cord nerve cells in animals at the Montreal General Hospital in 1980. This breakthrough has had a huge impact on efforts to prevent permanent disability following brain injury, stroke, and neuro-degenerative disease.
- University of Toronto researcher **Tak Mak** discovered T-cell receptors in 1983, and went on to clone and sequence the gene for these receptors. He describes T-cells as "biodetectives," cruising through blood and tissues looking for viruses to destroy. The receptors tell them when they have hit their viral target.
- Another University of Toronto researcher, **Lap-Chee Tsui**, discovered the gene that causes cystic fibrosis in 1989. His work is now the basis of international research efforts to find a cure for this disease, which affects one in every 2,500 children born in Canada.
- As the founder of the McConnell Brain Imaging Centre in the 1980s, **Brenda Milner** has focused on reducing damage to language skills caused by brain surgery.

The 1990s: New challenges, new responses

The 1990s brought new challenges and new opportunities. A strategic planning exercise in 1991, involving extensive consultations and workshops, brought together more than 4,000 members of the health research community across the country. The Council's resulting 1993 strategic plan, *Investing in Canada's Health*, featured two foci for MRC:

- First, funding support would be extended to include the full range of health research, including psycho-social factors related to health, population health, health services and health care delivery. In effect, MRC set out to become a broad health research council.
- Second, alliances and partnerships with a variety of organizations, including the private sector, would become a key strategy for attracting urgently needed new resources to support research across the country.

These developments are discussed in greater detail in later chapters.

MRC's leadership and growth throughout the 1980s was recognized in 1985 by Winnipeg's St. Boniface General Hospital Research Foundation, which bestowed on the Council its International Award for significant contributions to the development and support of research in medicine, pharmacy and dentistry across the country over its 25 years of existence.

Into the 1990s

- **Phillipe Gros**, of McGill University, and **Emil Skamene,** of Montreal General Hospital, have isolated a gene believed to be responsible for allowing the body to fight off a host of infections, including tuberculosis, salmonella, and leprosy. Their discovery holds the promise of finding new ways to counter such diseases and raises the possibility of making use of sophisticated gene therapy to enhance the body's disease-fighting powers.
- Nearly four million Canadians over the age of 15 have chronic pain problems, and many cannot get access to the limited number of specialized pain treatment services. **Sandra Lefort** has worked with a team at Memorial University and the University of Toronto to develop the Chronic Pain Self-Management Program, a 12-hour education program. The program has been successfully tested in St. John's, Newfoundland, and is being tested in four other locations before being made available nationally.
- **Frances Abbott**, of McGill University, is also focusing on pain. She is studying chemicals the body deploys to cope with injury and inflammation. Some of these chemicals appear to play a role in sending pain signals to the brain, and Dr. Abbott believes that one of these may be responsible for making pain last.
- **Judes Poirier**, of the Douglas Hospital in Montreal, has developed a blood test to determine a person's chances of developing Alzheimer's disease. The test can tell whether someone carries the "bad" gene — apolipoprotein — that is responsible for killing the neurons in the brain that control memory.
- **Leigh Field**, a researcher at the University of Calgary, has discovered two genes that produce susceptibility to juvenile onset, or Type 1, diabetes. This is the most severe form of the disease, requiring daily injections of insulin to stay alive. An estimated 100,000 Canadians have this form of the disease, which strikes one in 300 children.
- **Anne Bassett**, of Toronto's Queen Street Mental Health Centre, has followed a small number of families affected by schizophrenia over three generations. She and her team of researchers have found that the disease is inherited, and that it appears to worsen with each generation. Researchers believe several genes are responsible for affecting brain development in people with schizophrenia.

- **Alex McKenzie** and his colleagues at the University of Ottawa successfully isolated the gene associated with spinal muscular atrophy (SMA), a deadly neuromuscular disorder and the most common genetic cause of death among Canadian infants. Scientists believe the gene could one day be used in treating diseases ranging from Alzheimer's disease to some forms of cancer.
- **Cathy Logan**, of the University of Calgary, has identified two genes that may play a crucial role in the development of nerve cells that relay sensory information from the periphery of the body to the brain. She is studying these genes by introducing them into nerve cells where they are not present, and looking for changes in those cells. Her research could help in the development of therapies for birth defects such as spina bifida, as well as therapies to repair degenerating sensory systems.

A predominant feature of the 1990s was the federal government's efforts to fight the deficit. Despite the government's recognition of the importance of science and technology to the growth of Canada's economy, the research granting councils were not immune to deficit-related budget cuts. The federal budgets of 1995 and 1996 included a cut of 10 per cent from MRC's operating funds, followed by a further three per cent decrease in 1997. By 1998, MRC had lost $31 million in annual funding.

This placed particular pressure on MRC's ability to continue to fund excellent research at the same time that it had decided to expand its coverage to include other areas of health research. Less money had to be stretched in more directions.

The decision to actively pursue alliances and partnerships alleviated some of the pain. Additional funds were leveraged from other members of the health research community, including the voluntary and private sectors. Nevertheless, the impact of the budget cuts on basic research in particular was severe.

The Funding Gap

Throughout the 1990s, as MRC grappled with budget cuts, a "funding gap" emerged, with two key aspects:

- the difference between the number of excellent proposals approved for funding and the number that could be approved if sufficient funds were available;
- the difference between the amount of money peer review committees recommended that a particular grant should receive and the amount approved by MRC. Each year, funding levels were reduced in order to fund more grants.

In 1998-99, MRC was unable to fund 835 excellent proposals, representing a gap of $60 million. The average value of an MRC grant has increased 16 per cent since 1990, compared to more than 60 per cent in the United States.

The Canadian health research community was determined to keep Canada's health research funding at internationally competitive levels. It focused its efforts on convincing the federal government that restoring the budget cuts to research should be an immediate priority once the deficit fight was declared won. The government heeded the call, and, in its 1998 budget, restored MRC's core funding with an increase of $130 million over three years. Funding was also restored to the other two federal granting councils, the Natural Sciences and Engineering Research Council of Canada (NSERC) and the Social Sciences and Humanities Research Council of Canada (SSHRC).

Today, with a 1999-2000 budget of more than $300 million, MRC funds the research projects of more than 3,000 health scientists and provides salary support for more than 500 of the most outstanding. The Council also supports more than 2,700 Canadians as they train to become the researchers of tomorrow and, through project funding, finances the health research activities of nearly 10,000 Canadian scientists, technicians, and research assistants.

Throughout MRC's existence, peer review has been the backbone of the organization. Peer review has ensured that funded research meets internationally accepted standards of excellence. The MRC's peer review process has itself been recognized around the world as an exemplar of the "gold standard" of peer review.

All MRC research funding applications are subject to the MRC's internationally renowned peer review process. This independent review system for assessing applications involves the very best health scientists in Canada and around the world. More than 500 individuals volunteer their time and talents on more than 40 different peer review committees charged with reviewing

applications, while many more contribute written assessments of the strengths and weaknesses of individual proposals to assist the committees in their work. Their goal is to select the applications that demonstrate the greatest scientific merit and potential for contributions to knowledge. The criteria used to evaluate applications include: quality of the science, breadth of vision, originality of research, impact on the health of Canadians, feasibility, and potential attractiveness to collaborators and funding partners.

Following the decision to expand MRC's activities to encompass the full spectrum of health research, MRC Council created new peer review committees to enhance its ability to review research proposals in population health, determinants of health, health care delivery, health economics and other social and behavioural aspects of health.

The peer review system is the best available guarantee to government and to the Canadian public that taxpayers' dollars are being directed to science of the highest quality.

Health research: Part of our cultural identity

Canada is blessed with talented, hard-working researchers who get results far beyond their numbers and resources. As a nation, our accomplishments in health research far outweigh our small population and our limited investment. In fact, our impact on international research is significant:

Funding health research in Canada

MRC is but one of Canada's many funders of health research. At the federal level, MRC is the single largest funder, with a budget of more than $300 million. Several other federal bodies also contribute to the goal of achieving better health for Canadians:

- The **Natural Sciences and Engineering Research Council** spends about $10 million each year on health-related research in the life sciences, bioengineering, and medical devices.
- The **Social Sciences and Humanities Research Council** is estimated to spend about $3 million each year on the social, cultural, and behavioural aspects of health.
- **Health Canada** funds research in its own laboratories on the epidemiology and control of diseases, on the safety

of foods and medicaments, and on medical devices. As well, through the Health Transition Fund, it funds research on health care delivery.

- Within Health Canada, the **National Health Research and Development Program** spends about $12 million each year on health research priorities, including the determinants of health, the health impact of public policies, renewal and restructuring of the health care system, and the transfer and uptake of knowledge.
- The **Canada Foundation for Innovation** (CFI) was created in 1997 as an arm's-length organization funding research-related infrastructure in universities, hospitals, and research institutes. Since its creation, almost half of all CFI investments have been in the area of health research.
- The **Canadian Health Services Research Foundation** (CHSRF) was created in 1996, with an initial budget of $65 million over five years, increased to $100 million in the 1999 federal budget. CHSRF funds research on health systems.
- The **NURSE Fund**, announced in the 1999 federal budget, allocates $25 million to finance research on critical issues related to nursing and the delivery of health care. The Fund is administered by the CHSRF.

In addition, health charities, research foundations, the private sector, and provincial governments also provide funding for health research. In 1998-99, Statistics Canada estimated that $1.6 billion flowed into health R&D through these additional channels.

- Canada ranks fourth in the world in terms of publications per capita, ahead of both the United Kingdom (which is eighth) and the United States (ninth).
- Canada ranks first in the world in terms of citations per dollar spent on research.
- As measured by citations per paper published, Canada ranks second in the world in clinical research, fourth in biomedical research, and third in community health and social sciences relevant to health.
- Every year, Canadian researchers win more than half of all the grants that the U.S. National Institutes of Health (NIH) gives to foreign researchers. In 1998-99, Canadian researchers received US$17.5 million in grants from NIH; the seven other countries in the top eight recipients of international awards received a *total* of US$12 million among them.
- Canadian researchers were awarded 20 out of 47 (43 per cent) International Research Scholar awards by the Howard Hughes Medical Institute (HHMI) in 1997. These

awards provide support for five years to researchers who are judged to have the potential to make significant contributions to the study of basic biological processes or disease mechanisms. All of the Canadian winners of International Scholarships from the HHMI have received grant support from MRC, and are in turn training MRC research fellows or students.

Brett Finlay, a Professor of Biotechnology, Biochemistry, and Molecular Biology at the University of British Columbia, was selected as one of only two speakers from around the world for the Howard Hughes Medical Institute's Holiday Lecture on Science for 1999. The free lectures are broadcast live on the World Wide Web and by satellite to enable high school students to see and hear presentations by some of the world's leading biomedical researchers.

From the discovery of insulin in 1921 to today's multi-disciplinary research breakthroughs, health research in Canada has come a long way. As a result, most Canadians know someone who is alive and well thanks to advances in scientific knowledge — and someone who could not be cured because the knowledge has not yet advanced far enough. As well as supporting health research organizations such as the MRC through their federal tax dollars, Canadians contribute greatly to universities, hospitals, and other community organizations. This generosity clearly illustrates the importance we place on health, and our understanding of the fact that quality health care rests on the foundation of a strong research enterprise.

Continuing the tradition of excellence

MRC-funded researchers continue to make the discoveries that make a difference to the lives and health of Canadians and people around the world. The following are just some examples of the 3,000 researchers currently being funded by the MRC whose work will be encompassed in the new Canadian Institutes of Health Research.

- **Kristan Aronson**, of Queen's University, is comparing concentrations of certain environmental chemicals (such as pesticides, PCBs, and heavy metals) in the blood of men with prostate cancer and a control group of healthy men, to identify what, if any, role these chemicals may play in rising levels of the cancer. Her findings could help to design strategies to prevent this cancer.

- **Dr. Louis Delbaere** and his colleagues at the University of Saskatchewan have found a receptor site where a drug displaying potential anti-cancer properties binds to a key protein that helps to regulate cell propagation and growth. Their goal is to find a drug that will attack only cancerous cells, and leave healthy cells alone.
- **Mark Wainberg**, of McGill University, is focusing on how to combat HIV resistance to AZT and other drugs, in order to develop a comprehensive model of cost-effective care for treating HIV infection and disease.
- **Karl Riabowol** and **Igor Garkavtsev**, of the University of Calgary, discovered that an important gene is absent in cancer cells. This gene produces a substance that tells normal cells when to stop growing. When the two researchers exposed breast cancer cells to high levels of the gene products, the cancer cells stopped growing, leading to hopes for a technique to suppress the growth of cancer.
- **Ravi Menon,** at the University of Western Ontario, has been using Magnetic Resonance Imaging (MRI) to determine, with his colleagues in neurology, psychology, psychiatry, and physiology, how best to diagnose and treat patients with schizophrenia.
- **William Muller**, from McMaster University, is investigating two of the 20 to 30 cancer-causing genes. He has found that mutations in one of these genes are present in about one third of all human breast cancers, while mutations in the other are a factor in roughly half of all breast cancers. He is trying to find an agent that will block the gene and interfere with the process of tumour formation.
- **Janice Eng**, from the University of British Columbia, is studying what aspects of balance and gait problems experienced by people with Parkinson's disease would be helped by surgery.
- **Jeffrey Charuk, Reinhart Reithmeier,** and **Arthur Grey**, from the University of Toronto, have found that the same type of detergent found in commonly used household cleaners can reduce the amount of chemotherapy drugs required to treat multi-drug resistance. They discovered this while studying the role of a naturally occurring drug pump called P-glycoprotein that is found in high levels in the cell membranes of certain drug-resistant cancer cells. Their discovery could offer a useful adjunct to standard chemotherapy treatments.

- **Peggy Olive**, of the B.C. Cancer Research Centre, is seeking to understand how chromatin organization influences the ability of cells to repair damage caused by ionizing radiation. Evidence indicates that 30 to 40 per cent of tumours are resistant to killing by certain kinds of radiation. Discovering the mechanism behind this cell structure-related resistance can help in detecting tumours with this kind of resistance, measuring intrinsic tumour radiosensitivity, and providing new approaches to improving tumour response to radiation therapy.
- **Proton Rahman** is studying 60 Newfoundland families to find the gene that causes psoriatic arthritis — a less common form of arthritis that affects men and women between the ages of 20 and 50, and that is 10 per cent more common in Newfoundland than in the rest of the Caucasian population. His ultimate goal is to find a cure for the condition.

Chapter 2: Supporting Excellence for 40 Years

Investment in health research is, first and foremost, an investment in people. Over the past 40 years, MRC has invested close to $4.5 billion in Canada's best and brightest health researchers, generating new knowledge that has improved the health of Canadians and of people around the world.

Over its 40–year existence, the MRC has bestowed 66,450 operating grants and 47,434 personnel awards on excellent Canadian researchers. Over that period, an estimated 300,000 person-year positions (scientists, technicians, and research support staff) have been supported by the MRC.

MRC Annual Grants and Expenditures

	Operating Grants	Personnel and Other Grants & Awards	Equipment Grants
1990s	23,487	20,672	940
1980s	18,991	14,587	1,114
1970s	15,167	9,134	589
1960s	6,805	3,041	767
Total	**66,450**	**47,434**	**3,410**

MRC invests in health researchers through two channels:

- **Awards** in the form of salary support and support for research training. These awards support individual scientists in their work. They help to build capacity in the health research enterprise, ensuring that there is a critical mass of excellent health researchers who are encouraged and supported to apply their knowledge, skills, and creativity to the conundrum of health.
- **Grants** for specific research proposals support basic, applied, and clinical research projects in the health sciences, as proposed and carried out by investigators in laboratories in Canadian universities and their affiliated research institutes. These grants generate the knowledge and discoveries that lead to new ways to prevent ill health and disease, and new ways to treat them when they occur.

Building a dynamic, ongoing health research enterprise must be a sustained affair. Regular, ongoing funding is needed to ensure its continued success. Over 40 years, MRC has provided the continuity of funding that has enabled researchers to achieve their best — right here in Canada.

Awards: Building research capacity throughout Canada

"Throughout my professional life in Canada, the MRC has been an important source of my research funding and the main source of my professional income, first as a Research Assistant on a project grant to a colleague, and, from 1968 to 1993, as an MRC Research Associate .... I salute the MRC for its short-term investment in curiosity-driven research, and for its long-term investment in personnel. The outcome of the latter is harder to evaluate, but in the long run is, I believe, as important in establishing a culture of scientific enquiry as it is an integral component of medical teaching and practice."

Margaret R. Becklake

The cycle of research innovation begins with students. Without the initial fascination to which so many researchers attribute their initial attraction to science, without the initial harnessing of that fascination, there would be no health research enterprise in Canada. MRC is the one health research funder in Canada that has consistently supported researchers from the earliest stages of their careers. In the past ten years alone, more than 7,300 researchers have received MRC awards.

Queen Elizabeth II Fund

In 1959, to commemorate the visit of Queen Elizabeth II to Canada, Parliament established the Queen Elizabeth II Fund to Aid in Research on the Diseases of Children. Over its lifetime, the $1–million fund provided support for 11 Scientists for five-year terms in Canadian universities, and for 39 research trainees to conduct research into the causes, prevention, and treatment of diseases in children. The fund played an important role in the development of pediatric research in Canada. It was administered by a Board of Trustees, with administrative services provided by MRC.

Because the majority of health research in Canada takes place in universities, rather than in central research institutes, a way had to be found to support those researchers who wanted to devote themselves to research, rather than to the teaching and administrative work that most faculty members must undertake. Over the years, MRC has established several programs to recognize the best Canadian researchers at different stages of their careers, and to support their full-time involvement in research.

At the earliest phase, MRC studentships, such as the Farquharson Research Scholarships, provide funding for summer employment for medical students in research laboratories in hospitals and

universities across the country. In recent years, the Burroughs Wellcome Fund has provided support for awards to all Canadian schools of medicine, dentistry, pharmacy, and optometry to give undergraduate students exposure to research. Doctoral research awards are another source of support for graduate-level studies toward an M.S.C. or Ph.D.

Researchers who have completed their doctoral degrees are eligible for post-doctoral fellowships. These permit recent graduates to pursue research under the guidance of an established mentor, publish their research findings, and work toward establishing a career as an independent scientist.

Career-long support

Sergio Grinstein, of Toronto's Hospital for Sick Children, has received 13 years of personnel support, ranging from a fellowship in 1976-78 to the Distinguished Scientist award in 1997. He has also received five separate operating grants.

Richard Rachubinski, from the University of Alberta, has received 14 years of personnel support, including five years as an MRC Scientist (1992-97), in addition to his five operating grants.

These scientists are just two examples of excellent researchers who have been able to count on sustained support from MRC throughout their research careers.

The most prestigious fellowship award has been the **Centennial Fellowship,** which was offered for the first time in 1967. These fellowships were awarded to young researchers who had achieved special academic distinction to allow them to broaden their fields of interest and equip themselves for independent work in clinical investigation and interdisciplinary research. Up to 10 Centennial Fellowships were awarded each year, providing a unique opportunity for young investigators to expand their research horizons at a time when extended post-doctoral training was uncommon. In 1999, the Centennial Fellowships were converted into a unique award combining two years of senior post-doctoral support with two years of support for a first faculty position.

The current system of personnel awards for independent investigators began in 1975. Researchers can follow a path of staged five-year awards, from Scholar, to Scientist, to Senior Scientist, to Distinguished Scientist. Only the very best in each category are rewarded with promotion to the next category.

The MRC Research Career Ladder*

Recognition

Distinguished Scientist (20)
Senior Scientist (24)

Career Development

Scientist (81)
Scholarship (194)

Training

Fellowship (407)
Graduate Student Award (604)
Summer Research Award (305)

* *Numbers refer to 1998-1999*

"The Medical Research Council of Canada has supported my salary and research costs over the last 20 years, from when I started as a graduate student to the present."

Dr. Stephen Pelech
University of British Columbia

"It was not until 1998, when I received an MRC Scientist Award, that for the first time I have been able to stop worrying about finding salary support. Now I am able to devote my time to my research and to mentoring my trainees and other young investigators."

Dr. Rosemary Tannock

Scholarships were created in 1962 to support researchers assuming their first faculty appointments. The award, which is limited to five years, permits trained investigators to develop their ability to initiate and carry out independent research unhampered by the heavy teaching duties often expected of regular faculty members. MRC Scholarships have been the first step in the successful careers of many of Canada's outstanding health researchers of today.

The **MRC Scientist** program was created in 1982 to allow outstanding scientists with proven research accomplishments to devote themselves to full-time research. The program, which is aimed at established researchers, was designed to provide an increased number of research career positions over and above those provided by Scholarships.

Associateships, the most senior level of support, were first offered in 1956. These lifetime awards, renewable every five years, were designed to facilitate long-term planning and development of research in the health sciences in Canadian universities, and were awarded to a limited number of individuals of outstanding ability and training. These awards, later known as Career Investigators Awards, were discontinued in 1975, and terminated at the end of 1999.

The **Senior Scientist Program**, which has replaced the Associateship/Career Investigator Program, is designed to contribute to the salaries of scientists of exceptional merit who are leaders in their field. It is intended to support researchers with nine to 15 years of experience.

Nobel Laureate **Michael Smith** has been an associate/career investigator with MRC since 1966. He is currently the Killam University Professor and Peter Wall Distinguished Professor of Biotechnology at the University of British Columbia and Director of the Genome Sequence Centre at the British Columbia Cancer Research Centre in Vancouver.

Other noted MRC associates/career investigators include:

- **Charles T. Beer**, known for his research in isolating and purifying vinblastine, the first member of a new class of clinically useful anti-cancer agents
- **Margaret R. Becklake**, who has focused on the epidemiology of airway disease
- **Thomas Ming Swi Chang**, who has been supported in his research into artificial cells with an MRC Fellowship, Scholar Award and Associateship

The **Distinguished Scientists** Awards provide world-class researchers who have 15 to 20 years of experience with the opportunity to focus on specific research problems. These are individuals who constantly challenge accepted models and theories. They undertake unending expansion and reformulation of their work to incorporate the newest techniques and research findings. They are exceptional in the quality of their reputation internationally, and the strength of their collaborations around the world.

From promising newcomers to Canada's internationally renowned scientific pioneers, the MRC is proud of its role as a primary generator of research capacity in Canada and a significant contributor to the cycle of innovation.

MRC Distinguished Scientists:

1999:

Norman Boyd, University of Toronto
Joseph Culotti, University of Toronto, Samuel Lunenfeld Research Institute, Mount Sinai Hospital
Bodh Jugdutt, University of Alberta
Amira Klip, University of Toronto, Hospital for Sick Children
Jack Siemiatycki, Université du Québec, Institut national de la recherche scientifique, Institut Armand Frappier

1998:

George Chaconas, University of Western Ontario
Patrick McGrath, Dalhousie University
Anthony Pawson, Samuel J. Lunenfeld Research Institute

1997:

Harold Atwood, University of Toronto
Chris Bleakley, University of Alberta
Brenda Gallie, University of Toronto
Sergio Grinstein, University of Toronto
Michael Kramer, McGill University
Léon Sanche, Sherbrooke University

1996:

Robert French, University of Calgary
Fernand Labrie, Centre de recherche du Centre hopitalier de l'Université de Laval

Yogesh Patel, McGill University
Janet Rossant, University of Toronto
Nahum Sonenberg, McGill University

1995:

Jack Greenblatt, Charles H. Best Institute, University of Toronto
Robert Hancock, Bacteriological Diseases NCE, University of British Columbia
Léo Renaud, Loeb Medical Research Institute, University of Ottawa
Nabil Seidah, Clinical Research Institute, Université de Montréal
Charles Scriver, McGill University

Michael Smith Award for Excellence

Dr. Michael Smith

In 1993, Dr. Michael Smith, a renowned MRC Career Investigator, was awarded the Nobel Prize for Chemistry for his discovery and development of a technique called site-directed mutagenesis, which is used in genetic engineering. The MRC has recognized Dr. Smith's lifelong commitment to science and to encouraging other health researchers by creating the Michael Smith Award for Excellence.

The award, which consists of a medal plus $50,000 to be used by the awardee to further his or her research program, is presented annually to an outstanding Canadian investigator with fewer than 12 years experience, but who has demonstrated innovation, creativity, and dedication to health research. Recipients of the Michael Smith Award for Excellence are:

1999: **Michael Tyers**, Samuel Lunenfeld Research Institute, Mount Sinai Hospital
1998: **David Naylor**, Institute of Clinical Evaluative Sciences, Toronto
1997: **John Dick**, Hospital for Sick Children
1996: **Peter St. George-Hyslop**, University of Toronto
1995: **John Waller**, University of Calgary
1994: **Philippe Gros**, McGill University

Grants: Generating new knowledge

Basic, curiosity-driven research, is at the heart of the health research enterprise. It is research that asks original questions in the pursuit of new knowledge. It is the foundation upon which all other research develops. Basic research is carried out by researchers with a vision, and the determination to test their vision. The result is fundamental knowledge that helps to solve some of the world's most pressing problems. It is this important research that is at the heart of the MRC grants program.

Basic research is a long-term investment that may bear fruit only after many years of work. MRC funds grants over several years — up to seven years for some clinical trials — so that investigators have the security they need to carry out difficult research that may not yield immediate results.

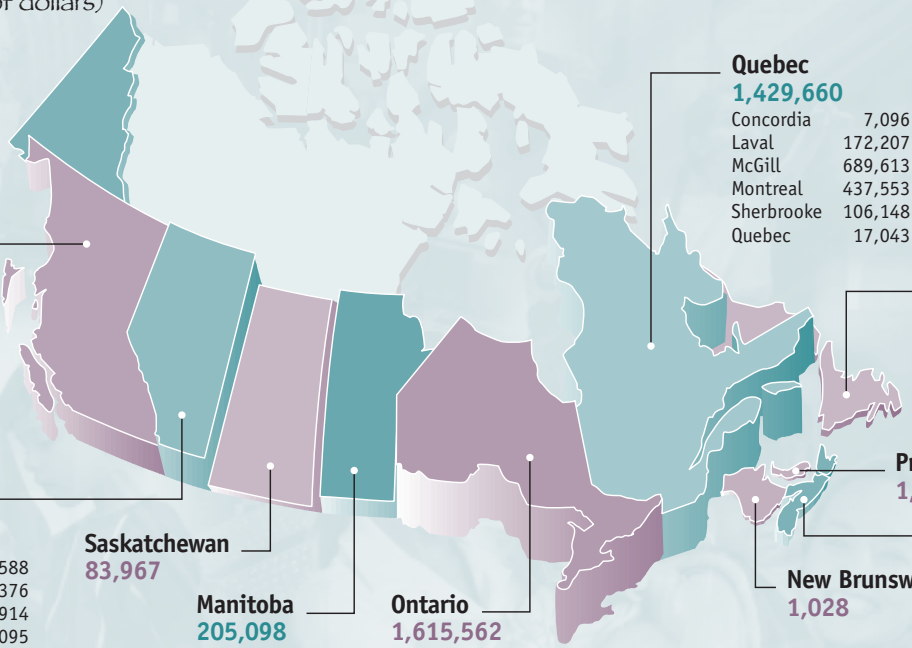
The majority of MRC grants are awarded to researchers affiliated with one of the 16 universities in Canada with medical schools. Health research, however, covers a wide spectrum, and health researchers can also be found in many other faculties in other universities, including nursing, rehabilitation therapy, dentistry, pharmacy, psychology, sociology, and economics. Thus, MRC-funded researchers can be found at the University of Toronto, McGill University, Dalhousie University, and the University of British Columbia — but also at the University College of the Cariboo in British Columbia, Alberta's Lethbridge University, Ontario's Trent University, and the University of Prince Edward Island.

Given the wide spectrum of disciplines that health research encompasses, it is not surprising that, at the country's 16 universities with medical schools, 55 per cent of *all* university research dollars are invested in the area of health — a fact that underscores how support for health research is a fundamental value among Canadians.

The following diagram illustrates the allocation of MRC grants and awards among Canada's universities and other research institutions over the past 40 years.

Allocation of MRC Grants and Awards 1960 - 1999

(in thousands of dollars)



British Columbia
410,773

Arthritis Society (B.C. & Yukon Div.)	40
University College of the Cariboo	160
UBC	397,820
Simon Fraser	3,910
Victoria	8,843

Alberta
445,973

Alberta Cancer Board	588
Alberta	266,376
Calgary	177,914
Lethbridge	1,095

Saskatchewan
83,967

Manitoba
205,098

Ontario
1,615,562

Brock	25
Carleton	3,826
Guelph	19,961
Lakehead	63
Laurentian	140
McMaster	210,592
NE Ont. Reg. Cancer Centre	272
Ottawa	131,531
Queen's	133,130
Ryerson	485
Toronto	866,804
Trent	765
Waterloo	6,460
Western	235,760
Windsor	257
York	5,491

Quebec
1,429,660

Concordia	7,096
Laval	172,207
McGill	689,613
Montreal	437,553
Sherbrooke	106,148
Quebec	17,043

Newfoundland
41,830

Prince Edward Island
1,034

New Brunswick
1,028

Nova Scotia
124,764

Dalhousie	124,636
Mount St. Vincent	49
St. Francis Xavier	9
St. Mary's	70

MRC continues to expand the research it supports, covering the full spectrum of health research, including basic biomedical, clinical, health services and health systems, behavioural and social determinants of health, psychological health, and population health. A brief look at recent research funded by MRC illustrates the importance of support for health research in improving the lives of Canadians:

Brain Function

- At the research centre of Hôpital Côte-des-Neiges in Montreal, a group directed by **André Roch Lecours** revealed new findings concerning the effects of aging on brain functions. Researchers have discovered that normal aging can have an impact on almost all aspects of linguistic behaviour.

- **Harold Robertson** of Dalhousie University is studying the phenomenon known as "kindling" that occurs when the brain works differently because of activity in the brain cells. Kindling is usually associated with a part of the brain called the hippocampus which has a central role in memory. Understanding kindling could teach us a great deal about epilepsy.

Cancer

- One of the major obstacles to curing many cancers is their ability to develop resistance to a wide range of drugs. **Susan Cole** and **Roger Deeley** of Queen's University found a gene that makes a protein which appears to be responsible for this drug resistance. By shutting off this gene, it is conceivable that the cancer cells would be rendered more vulnerable to conventional treatments.

- **Karl Riabowol** of the University of Calgary has discovered a gene that could shorten the life of cancer cells by eliminating them as they appear. His research focuses on finding out how cancer cells avoid this gene and discovering how to counter this phenomenon.

Cardiovascular Disease

- **Jack Hirsh** and his team of researchers at McMaster University are leaders in developing treatments for thrombosis. Their most noteworthy achievements include demonstrating that low molecular weight heparin and warfarin can effectively prevent deep venous thrombosis and pulmonary embolism.

- **Salim Yusuf** and his colleagues at McMaster reported this year in the HOPE Study that using beta blockers, aspirin, thrombolytic (clot-buster) agents and ACE-inhibitors (a special kind of blood pressure lowering agent), substantially improved survival after heart attack and lowered the risk of subsequent heart attacks. Yusuf is also part of the SHARE study (with the MRC and Heart and Stroke Foundation) which is examining 1,000 people from Toronto, Edmonton and Hamilton in an effort to find out if genetic or lifestyle differences are behind markedly differing risks for heart attacks among different ethnic groups.

Diabetes

- **Ji-Won Yoon**, at the University of Calgary, has found a trigger for diabetes — an enzyme produced in cells in the pancreas, called glutamic acid decarboxylase (GAD). Children who develop diabetes have an off-kilter immune system that allows the body's infection-fighting T-cells to attack the GAD enzyme when they should not, harming the pancreas and destroying the body's ability to produce enough insulin, resulting in Type 1 diabetes. He has developed a GAD vaccine for newborns that would build up a tolerance for the enzyme among T-cells and prevent them from destroying GAD later.

Genetics

- **Peter St George-Hyslop**, Professor of Medicine (Neurology) and Director of the Centre for Research in Neurodegenerative Diseases at the University of Toronto, was the first to demonstrate that Alzheimer's disease is not one single disorder. He and his team mapped and cloned a new family of genes called "presenilins" which, when mutated, are responsible not only for the aggressive early form of the disease, but also play an important role in all of its other forms.

Infectious Diseases

- Viruses that infect animals as well as people can have repercussions on human health. **Lorne Babiuk**, of the University of Saskatchewan, is studying viruses such as herpes in order to discover how they infect cells, how animal organisms react to them and what role genes play in the process. The results of this research should provide a better understanding of this disease among humans.

- Researchers at the University of Manitoba led by **Francis Allan Plummer** are studying individuals who appear to have immunity to HIV infection, a discovery which may advance

research on HIV vaccines. They are now trying to find a genetic factor that makes some people resistant to the HIV virus.

Motor Functions

- **Yves Lamarre** and a team of researchers at the Université de Montréal are studying motor diseases in the hope of developing better treatments to control tremors, and gaining new knowledge of normal motor functions and motor learning.

- University of Alberta researchers **Richard Stein** and **Arthur Prochazka** are pioneers in the emerging field of functional electrical stimulation. Stein's research has led to the development of electrodes that can be implanted beneath the skin in order to establish permanent transmission of electrical signals between deep muscles and myo-electric prosthetic devices. This "touch control" technique has enabled amputee musicians to continue to play. Prochazka has designed a bionic glove for quadriplegics that stimulates the muscles and nerves of the wrist in order to trigger thumb and index opening and closing motions.

Public Health

- One out of five Canadian families is a single-parent family, usually headed by a woman. **Marilyn Ford-Gilboe** and a team of researchers from the University of Western Ontario and the University of New Brunswick are studying the health of these families, particularly those broken up by violence or emotional abuse. The results of this study will make it possible to develop health programs and policies to support family health.

- **Katherine Gray-Donald, Noreen Willows** and **Johanne Morel** of McGill University are currently trying to discover the cause of anemia in Cree infants. In the northern Quebec region east of James Bay, Cree babies are four times more likely to be anemic than are babies born to urban, middle-class Canadian families and eight times more likely to have severe anemia. This research should contribute to the treatment and prevention of such anemia.

Did you know...

That the child-proof medication cap was created by a Canadian pediatrician?

Dr. Henri Breault practised medicine for 41 years in Windsor. As Director of the Poison Control Centre at the city's Hotel Dieu Hospital, he daily saw cases of children poisoned by medications in the home. He developed the child-proof cap in response. One year after its introduction, deaths by poisoning in the Windsor area alone were down by 90 per cent.

Dr. Breault was inducted into the Canadian Medical Hall of Fame in 1997.