

The National

Fetal-Neonatal Symposium

Workshop Report

1. Introduction

The National Fetal and Neonatal Research Consortium arose out of discussions surrounding the establishment of the proposed Canadian Health Research Institute for Mothers, Children and Youth (CHRIMCY), and in response to the MRC New Opportunities Program announced during the Spring of 1999. A self-funded workshop was held in Toronto on June 20th, 1999. This led to several developments: the formation of a provincial steering committee; the choice of the Banff Springs Hotel as a site where collegiality and camaraderie could be nurtured amongst participants working in different areas and aspects of perinatology; identification of 6 major themes where there was obviously existing strength and expertise within Canada; application and subsequent funding through the MRC New Opportunity Program from the August 1, 1999 competition. The 6 themes chosen for the workshop each had two co-chairs as follows: - Growth and Development (David Hill, Shoo Lee), Lung (Martin Post, Jacques Belik), Cardiovascular development (Harry Bard, Sandy Davidge), Brain and Neuron Development (Sylvain Chemtob, Bryan Richardson), Placenta (Jay Cross, Don Morrish), Preterm labor (Steve Lye, Peter Mitchell). The **objectives** of the consortium were to: (1) delineate the extent of the disease/condition internationally and in Canada.; (2) delineate the current major areas of research activity in Canada; (3) identify potential new areas for investigation, that might be the basis of one or more requests for application (RFA) to an appropriate CIHR institute; (4) develop strategies for achieving the objectives listed under item (3). The steering committee identified potential attendees from each of the 4 CIHR sectors across Canada, developed mechanisms to advertise the consortium extensively, and sought participation from non-Government organizations, professional organizations, Federal and Provincial funding agencies, industry and from trainees. In addition, five internationally recognized investigators (three from the USA, one each from the UK and from New Zealand) were invited to attend the workshop to provide critical input and comment. The final list of participants to the workshop, is listed under Item 3. Financial support was provided through the MRC New Opportunity Program, from AHFMR, Health Canada, PerkinElmer Wallac, MRC Groups in Perinatology and Child Health Research Institutes across the country.

The consortium workshop was held January 14-16th at the Banff Springs Hotel. Delegates were welcomed by Dr. David Olson, Director of the Perinatal Research Center at the University of Alberta. Project Leader, Dr. John Challis, gave a brief overview of the background and objectives of the meeting. Dr. Matt Spence, President and CEO of AHFMR and a member of the Interim Governing Council of CIHR, then provided an introductory overview presentation in which he described CIHR and its objectives, and he responded subsequently to questions from delegates. The working groups met in separate session and in plenary session to consider a precirculated list of topics and questions, that provided a framework for the group discussions. The reports and responses of the groups follow.

1. Workshop

- Description (Program as Appendix 1)
- Objectives

(i) The **long-term objective** of the workshop was to establish a national research base and infrastructure in fetal and neonatal health. The Canadian network will set the standard internationally. It will develop mechanisms to enhance basic and clinical health research efforts and translation of these into better care and outcomes for pregnant mothers, their fetuses and newborns. As a country, Canada should be able to guarantee the very best possible start to life for all its citizens that will ensure that every child has the ability to achieve her/his potential.

(ii) The **short-term objective** of the *National Fetal-Neonatal Research Consortium Workshop* was to bring together investigators in key areas of fetal and neonatal health in order to identify current strengths, discuss and plan new areas of research; recognize and promote opportunities for interdisciplinary and national, and international collaboration, extend the breadth of fetal and neonatal across Canada, and to establish new and innovative training programs for graduate students, post-doctoral clinical trainees that recognize national needs, strengths and excellence.

3. Participants:

LASTNAME	FIRSTNAME	UNIVERSITY/INSTITUTE	CITY	GROUP
Adamson	Lee	University of Toronto	Toronto	CV
Alvaro	Ruben C.	University of Manitoba	Winnipeg	Lung
Armson	Anthony B.	Dalhousie University	Halifax	Preterm
Bard	Harry	University of Montreal	Montreal	SC-CV
Barker	David	University of Southampton	Southampton	IR-Growth
Belik	Jaques	University of Calgary	Calgary	SC-Lung
Bocking	Alan D.	University of Western Ontario	London	WC-Preterm
Brochu	Michele	University of Montreal	Montreal	Growth
Campbell	Karen	University of Western Ontario	London	Preterm
Caniggia	Isabella	University of Toronto	Toronto	Placenta
Challis	John	University of Toronto	Toronto	WC-Preterm
Chan	Kevin	University of British Columbia	Vancouver	TR-Growth
Chance	Graham	Canadian Institute of Child Health	Goderich	NGO-Brain
Chemtob	Sylvain	University of Montreal	Montreal	SC-Brain
Cook	Jocelynn	University of Alberta	Edmonton	TR-Preterm
Cross	Jay	University of Toronto	Toronto	SC-Placenta

LASTNAME	FIRSTNAME	UNIVERSITY/INSTITUTE	CITY	GROUP
Davidge	Sandy	University of Alberta	Edmonton	SC-CV
Delvin	Edgard	University of Montreal	Montreal	Growth
Di Schiavi	Claudia	PerkinElmer Wallac	St. Laurent	IND-Brain
Drummond	Jane	University of Alberta	Edmonton	CC-Preterm
Dzakpasu	Susie	Health Canada	Ottawa	GOV-Growth
Fraser	William	Laval University	Quebec	CV
Gagnon	Robert	University of Western Ontario	London	Growth
Gibb	William	University of Ottawa	Ottawa	WC-Preterm
Gluckman	Peter	University of Auckland	Auckland	IR-Brain
Goodyer	Cynthia	McGill University	Montreal	Growth
Goodyer	Paul	McGill University	Montreal	Growth
Graham	Charles	Queen's University	Kingston	Placenta
Gratton	Robert	University of Western Ontario	London	Placenta
Greer	John	University of Alberta	Edmonton	Lung
Gruslin	Andree	University of Ottawa	Ottawa	Placenta
Guilbert	Larry	University of Alberta	Edmonton	Placenta
Guyda	Harvey	McGill University	Montreal	Growth
Halstead	Catherine	University of British Columbia	Vancouver	Placenta

LASTNAME	FIRSTNAME	UNIVERSITY/INSTITUTE	CITY	GROUP
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Han	Victor	University of Western Ontario	London	WC-Growth
Hasan	Shabih	University of Calgary	Calgary	Brain
Hay	William	University of Colorado	Denver	IR-Growth
Hill	David	University of Western Ontario	London	SC-Growth
Hu	Jim	Hospital for Sick Children	Toronto	Lung
Kaplan	Feige	McGill University	Montreal	Lung
Kennedy	Tom	University of Western Ontario	London	CC-Placenta
Kim	Jai	Hospital for Sick Children	Toronto	TR-Lung
Kingdom	John	University of Toronto	Toronto	Placenta
Kramer	Michael S.	McGill University	Montreal	Preterm
Lala	Peeyush	University of Western Ontario	London	Placenta
Langlois	Sylvie	University of British Columbia	Vancouver	Growth
Leduc	Line	University of Montreal	Montreal	CV
Lee	Shoo	University of British Columbia	Vancouver	SC-Growth
Lye	Steve	University of Western Ontario	Toronto	SC-Preterm
MacCalman	Colin	University of British Columbia	Vancouver	Placenta
MacNab	Andrew J.	University of British Columbia	Vancouver	Brain
Matthews	Stephen	University of Toronto	Toronto	Brain

LASTNAME	FIRSTNAME	UNIVERSITY/INSTITUTE	CITY	GROUP
McCourt	Catherine	Health Canada	Ottawa	GOV-Growth
McMillan	Douglas	University of Calgary	Calgary	NGO-Lung
McNamara	Helen	McGill University	Montreal	CV
Milne	Kenneth	SOGC	Ottawa	NGO-Placenta
Mitchell	Peter	University of Alberta	Edmonton	SC-Preterm
Morrish	Don	University of Alberta	Edmonton	SC-Placenta
Moutquin	Jean Marie	University of Sherbrooke	Sherbrooke	CV
Niday	Patricia	Perinatal Partnership Prog. of E & SE	Ottawa	CC-Preterm
Nimrod	Carl	University of Ottawa	Ottawa	CV
Olson	David	University of Alberta	Edmonton	WC-Lung
Orrbine	Elaine	Children's Hospital of Eastern Ontario	Ottawa	CHRICCY-CV
Piedboeuf	Bruno	Laval University	St. Foy	Lung
Post	Martin	Hospital for Sick Children	Toronto	SC-Lung
Praud	Jean-Paul	University of Sherbrooke	Sherbrooke	Lung
Richardson	Bryan	University of Western Ontario	London	SC-Brain
Roberts	James	University of Pittsburgh	Pittsburgh	IR-CV
Rurak	Dan	University of British Columbia	Vancouver	CV
Sauve	Reg	University of Calgary	Calgary	Brain

LASTNAME	FIRSTNAME	UNIVERSITY/INSTITUTE	CITY	GROUP
Shushan	Bori	PerkinElmer Wallac		IND-Brain
Smith	Graeme	Queen's University	Kingston	CV
Soderback	Patricia	PerkinElmer Wallac	Turku	IND-Brain
Spence	Matt	Alberta Heritage Foundation for Medical	Edmonton	NGO-
Sweezey	Neil	Hospital for Sick Children	Toronto	Lung
Thornburg	Kent	Oregon Health Science University	Portland	IR-CV
Tingle	Aubrey	University of British Columbia	Vancouver	WC-Brain
Torban	Elena	McGill University	Montreal	TR-CV
Vallance	Hilary	University of British Columbia	Vancouver	Growth
Van Aerde	John	University of Alberta	Edmonton	Growth
Walker	Dawn	Canadian Institute of Child Health		NGO-Brain
Watson	Carole	University of Western Ontario	London	TR-Brain
Wen	Shi Wu	Health Canada	Ottawa	GOV-Preterm
Whitfield	Michael F.	University of British Columbia	Vancouver	Growth
Wilson	Doug	University of British Columbia	Vancouver	Preterm
Windrim	Rory	University of Toronto	Toronto	Preterm
Yang	Kai-Ping	University of Western Ontario	London	Placenta
Yeger	Herman	Hospital for Sick Children	Toronto	Lung
Yuen	Doris E.	University of Ottawa	Ottawa	CC-Preterm

4. Background:

There are more than 5 million women of child-bearing age in Canada. Their offspring represent the future of this country. Many of those pregnancies, however, will become complicated by conditions such as pre-eclampsia (high blood pressure) (70% of pregnancies), diabetes (20% of pregnancies) and preterm delivery. Approximately 4% of babies are born small for gestational age. Preterm birth will occur in 7-10% of all pregnancies, leading to 75% of the early (neonatal) mortality and long-term disability including cerebral palsy, neurological and developmental handicap. Of particular concern are populations at great risk for preterm birth including aboriginal, teenage and certain cultural and socio-economic groups where the rates are even higher. The emotional stress for a family in which there is a preterm baby is high; the financial cost of health care has been estimated at more than \$200,000 for each very premature baby nurtured within a neonatal intensive care unit. Furthermore, recent population studies have suggested that development in utero may determine predisposition to major adult-onset diseases, including Type 2 diabetes and hypertension. Thus, our adult health is predetermined in the womb, demonstrating the pervasive impact of perinatal health on the individual, family and society.

In Canada, we have an extraordinary opportunity to make a major impact on these figures. Across the country we have nodes of excellence in various areas of fetal and neonatal research. The establishment of the Canadian Institutes of Health Research creates an environment that will bring together investigators, and will forge links with health care providers in improving the quality of maternal, fetal and newborn health.

Canada has already had major success in this arena. The late Dr. John Patrick of London, Ontario, was a pioneer in developing innovative methods of fetal surveillance in utero. Drs. Goran Enhorning and Fred Possmayer developed forms of surfactant that are used today for stabilizing the lungs of prematurely delivered babies, allowing them to breathe more easily. Canadian investigators have made major contributions to our understanding of the processes of fertilization, implantation and the birth process. At present there are three MRC groups working in the area of fetal and neonatal health. There are major research centres in Vancouver, Edmonton, London, Toronto and Montreal. We identified more than 100 potential participants in the National Workshop, each of whom is currently a recipient of peer-review funding for studies related to pregnancy, embryonic and fetal development, birth and the newborn period. This Workshop, stimulated by CIHR will bring these investigators to a common forum for the first time, at a National Planning Conference. We recognized that this national research strength was present largely in basic science, obstetric and neonatal departments from a limited number of universities, and that representation from a broader perspective of health science disciplines would be desirable. The Workshop therefore included participants from all CIHR cross-cutting research divisions and from a larger number of universities, coast-to-coast, in order to discuss broadening fetal-neonatal research linkages. By coming together, building trust and communicating more easily and effectively, we realize that we could do much more.

RESEARCH IN FETAL AND NEONATAL HEALTH IS INTERDISCIPLINARY AND INTEGRATIVE. THE "HOME" INSTITUTE FOR MANY MEMBERS OF THIS CONSORTIUM WILL BE THE CANADIAN HEALTH RESEARCH INSTITUTE FOR MOTHERS, CHILD AND YOUTH (CHRCM). HOWEVER, THE NATURE OF THE PROBLEMS WE FACE REQUIRES THAT MEMBERSHIP IN THE FETAL-NEONATAL RESEARCH CONSORTIUM WILL ACCRUE FROM INSTITUTES WITH PORTFOLIOS DEALING WITH WOMEN'S HEALTH; DIABETES, OBESITY, NUTRITION AND ENDOCRINOLOGY (DORIS); CARDIOVASCULAR DISEASE; RESPIRATORY DISEASE; MICROBIOLOGY AND IMMUNOLOGY; AND NEUROLOGICAL SCIENCES. THE DISCIPLINE IS BOTH HORIZONTALLY AND VERTICALLY CROSS-CULTURED.

5. Rationale

Complications of pregnancy, birth and the newborn period affect 5-10% of all gestations, and may underlie some adult disease states. Canadian investigators have achieved international recognition for contributions in these areas, but the potential to do more, afforded through CIHR, is extraordinary. The first National Fetal-Neonatal Consortium Workshop brought together these individuals to facilitate development of interdisciplinary and interactive research endeavours. The coordinating committee elected to pursue those areas of fetal-neonatal development where (a) the country currently has recognized major strengths; (b) the impact of new advances on the long-term health of Canadians would be most substantial; (c) the need for training opportunities was recognized. We proposed a single, national workshop with plenary sessions of parallel working groups in areas of *growth and development, placenta, lung, cardiovascular, brain development* and *preterm labor*, to allow extensive and intensive interaction both within and between these areas with the objective of establishing a new overall research and health policy agenda. We sought to marshal our nation's resources to engage and fight Canadian health problems of low birth weight, poor antenatal nutrition, preterm labor, hypertension during pregnancy, and many others.

REPORTS OF THE RESEACH GROUPS

Perinatal Brain Research

Cardiovascular

Growth and Development

Lung

Placenta

Preterm Labour

PERINATAL BRAIN DEVELOPMENT AND INJURY

Introduction / Current state of knowledge:

A variety of improvements in maternal and neonatal care has led to marked increases in perinatal survival. But, morbidity has lagged significantly behind, particularly that related to neurological development. These include severe and less severe brain disorders, which have major impacts on well-being to the patients and families. The proportion of the population that suffers from brain disorders that have an early developmental genesis is remarkable. For instance, the prevalence of cerebral palsy is ~0.2%, mental retardation ~2.5% (2 standard deviations below the mean IQ), learning disabilities ~5%, and behavioural disorders ~5-20% (depending on population analysis). There is also increasing evidence that early insults during development affect future brain development, which may predispose to serious conditions such as autism, schizophrenia and violence. Altogether, this places an enormous psychological, social and financial stress to families.

A major cause of neurologic morbidity is hypoxic-ischemic brain injury. In the term infant, based on a number of epidemiological studies it is suggested that approximately 20% of such insults occur in the perinatal period, 10% postnatally and the balance is attributed to antenatal insults. It is now estimated that the preterm infant, especially very immature, contributes to an increasingly larger prevalence of these various neurological and neurodevelopmental problems as survival rises associated with its relatively increased morbidity; these estimates are further relevant when one considers that the rate of severe prematurity (VLBW) has risen steadily over the last 15 years in North America (Dec. 1998 figures: 1.4% of births in USA). Furthermore, ventricular hemorrhages account for major causes of neurological insults in the preterm infant afflicting ~20-25% of VLBW. For purposes of illustration the estimated yearly costs simply of prematurity and special programs needed to deal with their disabilities are presented below. Additional lifetime costs need to be accounted for; it should also be pointed out that although USA data are quite accurate, Canadian data need to be reinforced with further studies. Data for estimated yearly costs incurred for cerebral palsy, mental retardation, learning disabilities and behavioural disorders amount to ~\$0.7 x 10¹² (USA) and \$50 x 10⁹ (CANADA). These sums which are simply for a portion of neurodevelopmental problems, amount to more than \$55 x 10⁹; in comparison, a high incidence (>10% population) important and steadily increasing disorder of an aging population, namely osteoporosis, costs Canadians ~\$1 x 10⁹/year.

	USA (US \$)	Canada (CDN \$)
Direct hospitalization	\$3.9 x 10 ⁹	\$1 x 10 ⁹
Repeated hospitalization and surgery	\$0.6 x 10 ⁹	\$50 x 10 ⁶
Special education (cumulative last 15 years)	\$4.5 x 10 ⁹	\$1.9 x 10 ⁹

Central nervous system malformations have also become a relatively important problem as a result of the increasing perinatal and infant survival. A major malformation is neural tube defects including meningocele and meningocele represent the more common types (other than spina bifida occulta) and are associated in ~85% of cases with hydrocephalus; these afflict 0.2%. The estimated costs incurred by neural tube defects in Canada, which are accounted for by surgery, hospitalization/rehospitalization, physio- and occupational habilitation/therapy, are >\$30 X 10⁹/year (cumulative last 15 years).

The data presented above clearly outline that our *advances made so far in neurodevelopmental disorders are clearly insufficient and highlight the need to move forward into this next challenging frontier of neonatology-perinatology which is associated with major neurodevelopmental disorders.*

Current Canadian Research Excellence and Efforts:

Canada has been over the last 30 years a pioneer in innovative cutting-edge research in perinatology. Numerous examples can be pointed out such as work on surfactant since the 1960s which has led to the development of surfactant therapy, resulting in major improvement in survival, in introduction of safer respiratory stimulants with caffeine, and innovative approaches to biophysical assessment of the fetus. A tremendous force in neurological and neurosensory developments as well, including detection of specific genes involved in motor neuron degeneration (eg. Wernigg-Hoffman), identification of perinatal risk factors to neurodevelopmental abnormalities, and establishment of electrophysiological assessment parameters, to name a few. One identifies in Canada expertises in a variety of the sectors, including fetal physiology and circulation, brain development, fetal circulation, respiratory control, brain behaviour, pharmacology, epidemiology and health services; this highlights the cross-cutting investigator force in Canada, in basic biomedical and applied clinical sciences, as well as in health services and epidemiology.

Present research funding in the area of the perinatal brain from MRC and other Canadian agencies approximates \$2.5 million/year with much of this funding related to brain development including neurogenesis and brain plasticity, and to adverse development including that related to hypoxemia/asphyxia. While there has been a considerate research effort with centers of strength throughout the country there has been a lack of collaboration/communication amongst these centers related to perinatal brain research; to basic biomedical research versus clinical research versus health delivery services and population health determinants; and to study in the adult which is relevant to that in the perinatal period. The Fetal/Neonatal Research Consortium will provide a forum for promoting such collaborations/communications linking Canadian centres in perinatal research not only to each other but also to other relevant grouping including clinical trial and outcome investigators, government/social agencies and their databases, and to neuroscience investigators of the adult brain.

Major opportunities for new knowledge:

As a result of the seriousness of the neurological disorders mentioned above, a regroupment of cutting-edge investigators provides an outstanding opportunity to address these major disorders by concerted multi-disciplinary approach including biomedical and applied clinical, research respecting health systems, health services and health population, and social, cultural and environmental.

The major sectors for future research endeavors identified are:

1. Brain growth and development
2. Ante- and perinatal insults
3. Psychodevelopmental disorders

For each sector a number of **areas for future research** have been outlined. These are:

1. Biomedical research:
 - developmental biology
 - functional genomics; cell migration / death
 - environmental factors: nutrition, drugs, infectious agents, exogenous stimuli
2. Clinical research:
 - databases and networking
 - screening: gene, proteomics, imaging, function
 - environmental factors
 - clinical intervention
 - therapeutics: pharmacological targeting / surgical
3. Health systems, health services and health population:
 - databases (in connection with StatsCan, Health Canada, Northern Affairs)
 - intervention programs: regionalization, early intervention programs
 - follow-up programs: preterm, IUGR, IVH/PVL, sensorineural
4. Social, cultural and environmental:
 - vulnerable populations: eg. aboriginal, regional [rural], immigration, adolescents, economically disadvantaged, low education
 - databases
 - environmental factors: nutrition, drugs, infectious agents, exogenous stimuli, geographical
 - intervention programs - new evaluations
 - educational programs: population, government policy makers, health care providers

Research in these cutting-edge sectors, will altogether provide tremendous advances for improvement in health services, expedite cross-cutting research approaches, foster new developments in both biology and biotechnology, favor the development of novel therapeutics and finally result in improved health of Canadians.

Strategies to achieve future goals

The Fetal/Neonatal Research Consortium will provide a forum for the advancement of perinatal research related to the brain and other subject areas, bringing together biomedical, clinical and health service investigators, and supported by an active administrative structure and communication linkages. The Consortium will promote an active membership through its Web site, newsletter, workshops, and possibly an annual meeting. The Consortium will align itself with relevant and appropriate CIHR institutes providing broad-based scientific input to research strategies of these institutes, directions for future research leading to requests for study applications. The Consortium will also promote linkages/partnerships with a variety of government, institutes, institutions, industry, societies and agencies within Canada and internationally.

CARDIOVASCULAR

1. Incidence and costs

Cardiovascular complications that affect fetal/neonatal health are vast. Important areas that have a major impact on the Canadian Health system are listed below.

- Preeclampsia (a complex, multiorgan dysfunction of pregnancy)
- Congenital malformations
- Maternal cardiovascular disease (congenital or acquired)
- Effects of normal pregnancy on the maternal cardiovascular system
- Fetal events that lead to cardiovascular disease in later life
- Environmental influences on maternal/fetal vascular development (i.e. smoking, alcohol, drugs, etc)
- Fetal adaptation from intra-uterine to extra-uterine life (i.e. fetal hypoxia, ductus arteriosus, persistent pulmonary hypertension, meconium respiration)
- Maternal/fetal nutrition and long term cardiovascular effects (i.e. hypertension, coronary heart disease, diabetes)
- Placental vascular pathology.

The costs on health services can be divided into 4 phases (a) pregnancy; (b) parturition; (c) intensive neonatal care; and (d) long term care of neurologically handicapped children. The total cost at the present time is difficult to evaluate. We can however take the example of preeclampsia which would illustrate the magnitude of the cost on our health system. This syndrome, which occurs frequently, affects 5% of all pregnancies. This pathology is associated with an increase in maternal morbidity (increase Caesarian-sections), neonatal morbidity and mortality as well as long term neurological sequelae and cardiovascular disease during adult life. This syndrome is becoming more prevalent because of the evolution of our society where women are having their first baby at a later age which is a risk factor for preeclampsia. ***The model of preeclampsia can be used to illustrate how Canadian research can result in major benefits to our population.***

1. Current Canadian Research Effort

Research effort can be categorized into studying mechanisms, prevention, management and the follow-up of newborns (preterm and growth restricted infants) born to preeclamptic mothers. Current research in Canada include studies carried in several centers to further our knowledge in understanding the mechanisms which will lead to preventive measures. These efforts should decrease hospitalization of mothers by reducing the need for cesarean sections as well as decreasing the need for hospitalization for newborns by reducing the number of preterm and growth restricted infants. However, in order for success there is a need for collaborative research efforts between basic scientists, clinicians, health service providers and epidemiologists.

2. Major Opportunities for New Knowledge

The complications of pregnancy such as preeclampsia can serve as a model where there are major opportunities for enhancing research efforts across multiple disciplines that will ultimately lead to improved health to the population. Studies can be initiated prior to pregnancy, during placental development and throughout gestation. Research is needed in order to understand the impact of preeclampsia on the development of the fetal cardiovascular system as well as long-term outcomes of both fetus and mothers. Also of great importance is the fetal and newborn programming that may cause cardiovascular disease later in adult life. However, in order to improve outcomes from this serious syndrome of pregnancy, research will need to encompass basic and clinical science as well as health services and epidemiology.

For example, basic science studies are needed to further the understanding of the mechanisms of the maternal cardiovascular complications which should lead to the understanding the placental factors that effect the cardiovascular system of mothers and fetus. This new information will allow us to establish markers for early detection and prevention so that new therapy can be tested in clinical trials. Once the results of clinical trials are established the information will have to be translated in order to improve the health care of the mother and the newborn. This will provide the opportunity to evaluate health services to determine whether novel therapy has reached current medical practice. Population studies should then be carried out to evaluate the outcomes of mothers and their newborn infants. In addition, studies in preeclampsia can certainly be a stimulus to innovation of technology. For example, there could be development of diagnostic and imaging methods for evaluating cardiovascular systems of the mother, the placenta and the fetus.

3. Strategies for Filling Research Needs.

In order to make progress in this serious disease process (as well as other cardiovascular complications related to fetal/neonatal health), there is a need for:

- a system of salary support at all levels to encourage investigators in both basic science and clinical research.
- strategic initiative grants for operating funds.
- an infrastructure with databases accessible across Canada.

GROWTH AND DEVELOPMENT

Incidence and cost

Fetal growth and development presents both a perinatal and long-term burden on health care costs which has implications throughout life. Term IUGR, with an incidence of about 4% of births, presents immediate problems for neonatal medicine related to organ maturity. Additionally, it has been established that IUGR carries substantial risks for diseases of adulthood including diabetes, stroke, hypertension and osteoporosis. Work by David Barker and colleagues has shown that a strong inverse correlation exists between mortality from cardiovascular disease below age 65 and birth weight (1). Similarly, the relative risk for prevalence of syndrome X, consisting of type 2 diabetes, hypertension and hyperlipidaemia, is 18 fold higher in men born less than 2.5 kg compared to those over 4 kg. Low birth weight infants also carry increased risks of childhood behavioral problems and learning deficits with long-term societal implications. Clearly there must exist a programming of physiological and neurological axes in early life which are modulated by the intrauterine environment. The inappropriately large infant, such as the macrosomic baby born to the poorly controlled diabetic women, is also at risk from perinatal disease, such as functional immaturity of the lungs, and of metabolic disorders in later life. Diabetes complicates approximately 2% of births in Canada. Around 75% of small for gestational age infants have a pathology which arises in the second half of pregnancy as a result of the intrauterine environment. A further 7 - 10% of abnormally small for age infants have congenital anomalies arising in early development.

An understanding of the cellular, molecular and endocrine mechanisms governing the growth and maturation of individual organs and tissues is therefore essential to managing and potentially reversing the adverse implications of abnormal fetal growth.

Current Canadian Research Effort

Canada has a leading international position in research into the fundamental mechanisms of embryonic and fetal growth, development and physiology. Presently approximately 125 projects are funded by MRC at around \$10 million per year of which 20% deal with the mechanisms of cell growth and the actions of peptide growth factors, 26% examine early embryogenesis, morphogenesis and the origins of congenital abnormalities, 30% study fetal physiology, endocrinology and the mechanisms of IUGR, 7% research the fetal programming of adult diseases, and the remaining 17% deal with childhood growth and nutrition. Concentrations of basic research exist in South-West Ontario, with three MRC Groups which are already networked, Montreal, Edmonton and Vancouver. Strengths exist in the origins of IUGR, developmental biology of the brain, lung, heart, kidney, pituitary and adrenal, endocrine ontogeny and the impacts of intrauterine insults such as nutritional insufficiency and hypoxia on growth processes and endocrine pathways.

Canada has several successful, perinatal (Toronto, Quebec City, Sherbrooke) and neonatal (Vancouver, Edmonton, Hamilton, Toronto) groups which lead and conduct multi-centered clinical trials internationally. They lack central infrastructure and coordination. Strong cost evaluation expertise exists (Vancouver, Hamilton) but has not been widely applied to clinical trials. Canada is a leader in neonatal health services and policy research with research

coordinated by the Canadian NICU Network (Vancouver), with international collaboration. It has a national NICU database, which can be linked to other perinatal and health databases. Perinatal health services research groups exist in several centers (Vancouver, Toronto, Quebec City, Sherbrooke) but are not linked in their efforts. Knowledge information groups provide important support, including the Canadian Cochrane Collaboration (Toronto, Hamilton). Technology assessment is conducted by the Canadian Office for Health Technology Assessment (COHTA) and its provincial equivalents. There are well-established groups but uncoordinated groups studying preterm birth, long-term disabilities, and neonatal follow-up. Provincial surveillance programs and databases exist in BC, Alberta, Quebec and Nova Scotia. An effort to create a Canadian Perinatal Surveillance system is under way, but standardization of norms and definitions, and coordination of efforts is a major problem.

Major opportunities for new knowledge.

- 1) There is a need to build on our present strengths in mechanistic biology to identify when critical windows exist in fetal development for individual tissues and organs, how various animal models best represent the human situation, how environmental insults differentially affect organ growth processes, and where and when plasticity exists within these tissues to allow potential recovery. This will facilitate an understanding of the cellular and molecular origins of fetal programming of adult disease, and the origins of learning and behavioral problems in childhood. These studies should extend into childhood to investigate the physiological implications of catch-up growth.
- 2) The adequacy of the quality of maternal nutrition prior to and during pregnancy in Canada is unsure, particularly regarding micronutrients. The interactions between nutrition and embryonic and fetal gene expression during development needs additional study to identify important micronutrient components and their role in ontology and programming.
- 3) Since congenital anomalies are an important cause of fetal growth disorders there is the opportunity to capitalise on our national expertise in developmental biology, fetal physiology and genetics to discover the genetic and environmental origins of such anomalies, including effects of teratogens and environmental pollutants, alcohol and drugs. New molecular screening technologies should be used to identify affected individuals either pre-term or at birth; for instance the genomic and proteomic analysis of fetal cells in maternal blood.
- 4) Creation of targeted, longitudinal, birth cohort databases capable of providing in-depth clinical and outcomes information for examining impact of growth trends on metabolism, neural development, learning, behavior and cost implications, including the study of trans-generational consequences
- 5) Examination of post-delivery influences which affect outcomes, such as social, economic, parenting, nutrition, health care, education.
- 6) Translation of research into guidelines and implementation in practice

Strategies

- 1) Cross-cutting networks of investigators should be established to facilitate the transfer of knowledge on biological mechanisms of growth, and likely prevention or intervention strategies for abnormal growth, to human clinical trials and subsequent integration into health services practice. Since critical mass in basic science is strong the predominant capacity-building need is for increased, targeted operating funds via RFAs.
- 2) There should be a reassessment of what constitutes abnormal fetal growth in terms of definitions and diagnosis. There should be standardization of the accurate dating of gestational age in first trimester using ultrasound, and an appreciation of the importance of individual growth trajectory rather than absolute birth weight as a diagnostic tool. New advances in non-invasive diagnostics should be explored, such as functional magnetic resonance imaging and 3D ultrasound, to identify the extent of anatomical and metabolic dysfunction associated with abnormal growth trajectories. Standardization of fetal, infant and child databases and their integration within a national network will greatly facilitate our ability to evaluate intervention strategies.
- 3) Formation of groups in congenital anomalies, AIDS, clinical trials and health services research
- 4) Establish funding mechanisms to initiate and support longitudinal cohort studies that are capable of examining the impact of interventions developed by basic science research on clinical care, outcomes and costs
- 5) Establish on-going workshops and internet based systems to disseminate information and foster partnerships, and provide support which facilitates mentorship and provides training opportunities
- 6) Ensure appropriate peer review system capable of reviewing cross-cutting grant applications

LUNG: Perinatal Respiratory system

Incidence and Cost

- 90 % of admissions to neonatal care units are partially or totally related to respiratory problems
- 20% of premature infants go home on supplemental oxygen
- Cdn\$ 1.5 – 2.5 billion is the annual cost of caring for these infants

Current Research Effort

Major Research Thrusts:

- Developmental (Lung Immaturity: eg. surfactant deficiency, CLD)
- Congenital (eg. CDH, Surfactant protein Deficiency, Tracheal-Esophageal fistula, Alveoloa-Capillary Dysplasia, Alveolar Acinar Dysplasia)
- Vascular and Airway Reactivity (PPHN, Bronchospasm)
- Control of Breathing (Apnea of Prematurity and Hypoventilation Syndrome)

- Major areas of activity

	BASIC	CLINICAL	HEALTH	POP / EPIDEM.
DEVELOPMENT.	major	minor	minor	minor
CONGENITAL	?	?	?	?
VASCULAR	minor	minor	?	?
BREATHING	major	major	?	?

- Major research centers: Quebec, Ontario, Alberta
-

Major opportunities for new knowledge

Given the above identified weaknesses regarding research on the perinatal respiratory system the following strategic initiatives are suggested:

- **Lung development and congenital anomalies: a study of growth and maturation of the lung and the factors accounting for anomalies**

Rationale: There is an increase the identification of congenital lung anomalies with increased survival due to improved technological advances in neonatal and fetal care. There is limited knowledge in the area of growth and maturation in regards to the causative factors of congenital lung anomalies.

- **Regulation of Pulmonary vascular resistance in the transition from fetal to neonatal life.**

Rationale: Five percent of admissions to NICUs are related to PPHN. Little is known about the factors responsible for the maintenance of a high pulmonary vascular resistance during fetal life and the rapid decrease at birth.

- **Research on Provision of Health services in the community to infants discharged home with CLD and in need of supplemental oxygen.**

Rationale: Twenty percent of premature infants are discharged home on supplemental oxygen. The provision of health services to this population as well as issues such as best approach to wean supplemental oxygen and promote adequate nutrition and development have not been properly addressed.

- **Clinical research geared at the prevention of lung injury in premature infants and outcome research on the long term follow up of chronic lung disease in this population.**

Rationale: The incidence of CLD has dramatically increased with the survival of very low birth weight infants. Strategies to prevent lung injury and minimize the long term morbidity associated with this condition will have a great socioeconomic impact, as well as the quality of life for the premature infant population.

Strategies for enhancement of research output in the area of perinatal respiratory system:

General

- Establish a Canadian perinatal respiratory research network. This will provide the opportunity to strengthen collaboration, share information, establish data, material and tissue banks. Increase awareness of the training opportunities to prospective graduate and post-graduate students.
- Identify barriers and enhance training of basic sciences/clinical/population health investigators in the area.
- Increase public awareness of the morbidity and mortality associated with perinatal respiratory system diseases.

Specific

	RESEARCH NEEDS
BASIC	<ul style="list-style-type: none"> • Animal Models • Genetics / Genomics / proteomics • Bioinformatics • Imaging Technology
CLINICAL	<ul style="list-style-type: none"> • Consortium for Clinical Trials • Central Facility for patient accrual • Development of training programs and facilities for Clinician-Scientists in the

	area of Perinatal Lung Research.
HEALTH SERVICES	<ul style="list-style-type: none"> • Inventory of current resources and personnel • Introduction of new technologies and procedures into clinical practice and education.
POPULATION AND EPIDEMIOLOGY	<ul style="list-style-type: none"> • Development Integration and universal access of National Databases related to health and disease • Standardization of Clinical Outcome Parameters

THE PLACENTA in Feto-Neonatal Health and Disease

1. Placenta-Related Diseases of Pregnancy: Incidence and Costs

The central function of the placenta is to promote delivery of nutrients and oxygen to the fetus. *Abnormal placental development and function appears to be a primary causative factor in several diseases of pregnancy.* These abnormalities range from implantation (recurrent abortion) through development (preeclampsia, IUGR) to preterm labour and subsequent poor neurodevelopmental outcomes of affected infants.

- The prototypical example of this is preeclampsia (PE), a disease affecting about 3-4% of pregnancies. After delivery, preeclampsia remits, indicating a central causative role of the placenta. Intrauterine growth restriction (IUGR) occurs in 4% of all pregnancies and in many cases clearly involves defects in the placental structure and/or function. A significant fraction of these infants later show neurodevelopmental defects. Early embryonic mortality ('spontaneous' or 'missed' abortion) is commonly associated with defects in placental structure.
- The placenta is also a target for many environmental and maternal disease insults. Maternal smoking (and there is an increasing percentage of women who smoke) is correlated with increased stillbirths and placental complications of IUGR, placental abruption and placenta previa. There are multiple placental abnormalities induced by smoking, possibly linked through induction of hypoxia. Indeed, any factor restricting placental blood flow has long been known to adversely affect the fetus. Other external factors producing abnormalities include drug use, infections, and maternal disease such as diabetes (2% of pregnancies).
- Spontaneous preterm labour is a serious perinatal event occurring in 7-10% of pregnancies and accounting for 75% of neonatal morbidity and mortality. About half of preterm labour is initiated by premature rupture of the membranes, a component of the placenta. Signals produced by the placenta are thought to be involved in the onset of labour and therefore the placenta is an important potential therapeutic target for controlling the onset of labour. In some cases, defects in the placenta can be the precipitating event, as in cases of placental infection.
- As well, maternal immune tolerance of the feto-placental allograft is not well understood and is involved in recurrent abortions (0.8% of pregnancies) as well as responses to infections.
- There is also now known strong associations between low birth weight and the propensity to develop cardiovascular (e.g., hypertension) and metabolic (e.g., diabetes) disease in adulthood. This principle is now well established from epidemiologic studies in humans as well as experimental studies in animal models and suggests that placental abnormalities can impact on future disease.

Placental dysfunction is thus associated with or causes diseases comprising 20% of pregnancies.

2. Current Canadian Research Effort

Areas of existing critical mass and research strength at international levels are as follows:

- placental pathologies (D.Kalousek, UBC; J.Kingdom, U Toronto)

- implantation (T.Kennedy, UWO; G.Schultz, U of Calgary)
- regulation of trophoblast differentiation and biology (J.Cross, U Calgary; D.Morrish, U of Alberta; C.MacCalman, UBC; P.Lala, UWO; C.Graham, Queen's; I.Caniggia, U of Toronto; Y.Tremblay, Laval)
- endocrinology (J.Challis, U of Toronto; M.L.Duckworth, L. Murphy, U of Manitoba; A. Gruslin, W.Gibb, U of Ottawa; P.Leung, UBC; K.P.Yang, UWO; J.Lafond; U of Montreal)
- developmental mechanisms (J.Cross, J.Rossant, V.Giguere)
- human genetics (D.Kalousek, UBC; W.Robinson, UBC)
- immunology (A.Croy, Guelph; L.Guilbert, U of Alberta; M.Baines, McGill)
- large animal placentology (G.Foxcroft, W.Dixon, U of Alberta)

Particular note is of MRC Groups in Toronto (S.Lye, J.Rossant, J.Cross, L.Adamson, L.Langille, J. Kingdom, J. Challis), UWO – U Toronto (Lawson Research Institute (V.Han, B.Richardson, A.Bocking, R.Gagnon, D.Hill, P.Yang, G.Hammond, J.Challis, S.Lye). There is a strong Perinatal Research Centre at the University of Alberta (D.Olson, S.Davidge, P.Mitchell core members and 27 other affiliated researchers cutting across fields from basic science to health delivery).

Basic investigation is thus well represented across the spectrum of investigations, though each area has only 1-2 persons.

3. Need for Additional Research Effort

Despite the widely appreciated role of placental dysfunction in diseases of the fetus, neonate and mother, the underlying mechanisms are poorly understood. In addition, one of the tremendous 'missed opportunities' to date is that routine examination of placental function both by clinician and the pathologist is not widely practiced, even in academic Ob/Gyn centers. The latter deficiency has severely limited the progress in research efforts, precluded development of population based studies, and curtailed efforts to translate advances in research back into clinical practice.

Priority Research Directions:

- Population based studies to examine the incidence of different types of placental pathology in all cases of pregnancies complicated by PE and IUGR. It has become evident that PE, IUGR and 'missed abortion' can show distinct pathological features in the placenta that can likely be attributed directly to defects in different aspects of placental development. This implies that different types of underlying mechanisms need to be investigated. At a minimum, these studies should correlate these findings with clinical information and neonatal outcome. This goal should be realistic given the number of existing centers of excellence in academic perinatal medicine and Canada's well-funded healthcare system.
- Basic research aimed at identifying the mechanisms underlying the formation of placental villi. While the regulation of invasive trophoblast cells that are defective in PE is reasonably well understood, the formation of the placental villi and their underlying vascular network, are comparatively poorly understood and much less well studied in Canada and worldwide.
- Translational research is needed for extrapolation of information from animal models, particularly mice, to the human placenta. The molecular control of placental development is being elucidated at a rapid rate through genetic studies in mice. There is a tremendous

opportunity to use these insights to shape hypotheses about the molecular pathways that underlie human placental pathologies. The expertise in Canada is uniquely qualified to take a worldwide leadership role in this area.

- Integrated basic and clinically-based research is required to identify the most critical transport and endocrine functions that promote fetal growth and determine the potential importance of their dysfunction to IUGR.
- Integrated basic and clinically-based research is required to identify the placental contributions to maternal disease in PE. These factors will become the basis of prognostic tests and probable therapeutic targets for intervention.

4. Strategies for Filling Research Needs

- Strategic Grants – high priority and underdeveloped areas of research need to be addressed by special funding programs
- Capacity Building – there is urgent need for increasing the number of clinical research fellows and faculty who would provide the key links between basic research and the health care delivery system.
- Capacity Building - urgent need to increase the expertise in placental pathology and recognition of value of placental examination for understanding perinatal disease.
- Infrastructure – perinatal outcome databases should include information on placental function (e.g., placental weight, ultrasound assessment of uterine and umbilical blood flow) and placental pathology findings. In addition, there is a need for large-scale archiving of samples from IUGR and PE placentas to serve as a resource for molecular/genetic-clinical associations.

5. Important Links With Other Research Groups

a) International Collaborations

Need to maintain interactions with major centers of excellence in placental research in Germany (Drs. Kaufmann and Winterhager), England (Drs. Smith, Redman, Barker), USA (Fisher, Strauss). There are two proposed mechanisms to accomplish this:

- CIHR and partner-funded international workshops
- exchanges of trainees and visiting scientists
- establishment of international grant programs

b) Other Research Areas Within Canada

- Cardiovascular
- Genetics
- Embryology
- Immunology

c) Health Care Delivery System

- there is a need to promote the importance of research to future health care through lobby efforts to regional health authorities

PRETERM LABOUR

The Problem

Preterm birth is one of Canada's major health concerns. Every year in Canada, there are approximately 30,000 babies born prematurely, accounting for 7.1% of all births. Though this rate is lower than in most of the world, it is significantly higher than in Scandinavian countries, suggesting that there is room for improvement. Most disturbingly, the rate of preterm birth in Canada is increasing over the past two decades. Within Canada, there are obvious social and regional differences with the highest rates of preterm delivery occurring in the Northwest Territories and obvious clustering of cases within the lower socio-economic areas of cities.

Preterm birth is associated with most of the death and permanent disability arising from the birth process. Birth before the fetal organs are sufficiently mature to permit survival outside the womb leads to many immediate and long term health problems involving the lungs, brain, cardiovascular system and essentially every other organ system. The direct costs of care for these newborns in the few weeks after birth are close to \$1 billion annually. The costs of prenatal care and the costs of long term care, in the home or in institutions, for the children left with disabilities have been estimated to be at least \$3-4 billion annually. There are indirect costs arising from the medical and social sequelae of preterm birth, and substantial emotional and social consequences within a family experiencing a preterm birth.

Current Canadian Research Effort

For the purpose of discussion, the research issues regarding preterm labour were divided into 5 modules: determinants, mechanisms, diagnosis, therapy and outcomes. Canada has considerable strength and international recognition in all areas. Total operating funds from MRC for investigators primarily involved in research into preterm labour is estimated at \$10 million exclusive of personnel awards for investigators and trainees. We estimate that at least this amount comes from non-MRC funds including governmental and non-governmental funds from Canada and abroad.

Opportunities for New Knowledge

There was agreement that preterm birth is an event that is the end result of a diverse group of possible etiologies. Consideration of preterm birth as a homogeneous "disease state" may have led researchers to misinterpret their data and draw erroneous conclusions. Consideration of preterm birth by subgroup analysis according to gestational age or other clinical factors (presence of infection, multiple births) may provide important new insights.

Canada has considerable strength in the general area of Population Health regarding preterm birth. There are strong suggestions that factors such as socio-economic status, nutrition, stress, and working are determinants of preterm birth. However, the data are weak and there remains great controversy about the precise roles of these potentially modifiable factors,

particularly considering the specific sub-types of preterm birth. Identification of social factors predisposing to preterm birth may suggest social support programs to avoid the increased risk. Linkage to Health Policy organizations and other high level governmental agencies will be necessary to accomplish these tasks. There is immediate need and opportunity to investigate the relationship between genes and the environment, an area that may have particular relevance to preterm birth. Linkage with the other research sectors within the preterm labour field and in other research areas will facilitate further development of this research thrust.

Canada has several international leaders working in the area of regulation of the timing of birth, term and preterm. This provides a strong basis on which to build further research activity and interactions with other research sectors. More research is required to better understand the normal regulatory mechanisms of labour and delivery but attention must also be directed towards understanding pathological mechanisms that lead to preterm birth. Consideration must be given to different mechanisms of preterm birth in different clinical situations (multiple gestation, infection, bleeding, etc.). Early studies by Canadian investigators have suggested possible mechanisms by which uterine stretch (as in multiple gestation), stress or infection may cause preterm labour and there is great opportunity to move these studies forward quickly.

The diagnosis of preterm labour remains a major problem. Of those women who experience preterm contractions, only a minority actually will go on to deliver. There is tremendous need to develop a test to distinguish those in true labour from those who are in “false labour.” There are several tests available but none, individually, are clinically useful. Combinations of these tests may provide the diagnostic accuracy to distinguish those women who can be returned home to their own communities and families from those who require further hospitalization and treatment. Results of research in this area could lead to immediate changes in clinical practice that would spare the considerable health care resources expended on unnecessary hospitalization of these women. Development of new, more accurate and precise tests using gene chip technology is a realistic goal of Canada’s present research establishment.

Current treatment of preterm labour is quite unsatisfactory. Not only are many women (and their fetuses) treated needlessly as noted above, but treatment for those in true preterm labour is largely ineffective. New clinical trials are needed to test the effectiveness and safety of potential new therapeutic agents. Based on information from the groups studying the determinants and mechanisms of preterm labour, new therapeutic strategies can be designed to prevent preterm birth. “Targeted” pharmacological therapy and gene “knock-in” or “knock-out” therapy are areas that could be addressed in the immediate future.

Critical evaluation of all of the previously described projects is essential to support the validity of the conclusions. For any of the therapeutic trials, short term and long-term infant outcome data will be necessary to evaluate the risk/benefit ratios. There are pockets of expertise in Canada for these studies but there is need to bolster this effort with both professional expertise and operating funds, especially for the essential long-term (several years) studies. A national network is particularly important in this area.

Strategies to Exploit the Opportunities

Over the past decade, there has been a significant increase in knowledge within the individual research areas involved in preterm birth. Canadian investigators have made significant contributions to these advances. However, preterm birth has remained as the major clinical problem in maternal-child health. To ensure that the present opportunities are fully realized, a new paradigm is needed to integrate the research activities of the present Canadian research establishment. The Fetal-neonatal consortium within the CIHR is the ideal vehicle to accomplish these goals.

LINKAGES FOR CONSORTIUM ON FETAL AND NEONATAL RESEARCH

Ontario-Quebec Perinatal Group
Western Perinatal Group
Reproductive Development Workshop
Montreal Consortia
Society for Pediatric Research and affiliates
Placenta Group - North American Trophoblast Society
Perinatal Research Society
Endocrine Society
NICHD
Diabetic Pregnancy Study Group of the European Association for the Study of Diabetes
European Society for Perinatal Research
UK Royal Colleges
Cochrane Collaboration
Health Canada and branches
Statistics Canada
Provincial neonatal screening programs
Provincial Reproductive Care Programs
Provincial Birth Defects Registry
Canadian NICU Network database
College of Medical Genetics
SOGC
CPS
Foundation for Health Services Research
ICES, Toronto
CHEPA, McMaster
CHSPR, Vancouver
Perinatal Epidemiology Research Centers, Calgary, Toronto, Montreal, Quebec City, Sherbrooke
Centre for Community Health and Health Evaluation Research, Vancouver
HealNET (Network of Centres of Excellence), Hamilton
Canadian genetic diseases network (Network of Centres of Excellence), Vancouver
Population Health Institute, University of Ottawa
Disabilities Consortium - Eva Rosenbaum
Informatics Consortium
Pediatric Nutrition Consortium
Biochemical diseases consortium
U Victoria School of Health Informatics
Provincial administrative health databases

RECOMMENDATIONS FROM THE PANEL OF INTERNATIONAL ASSOCIATES

Prof. DJP Barker (University of Southampton, UK)

Prof. P.D. Gluckman (University of Auckland, New Zealand)

Prof. W. Hay (University of Colorado, Denver, CO)

Prof. J.M. Roberts (University of Pittsburgh, Magee Women's Hospital)

Prof. K. Thornburg (Oregon Health Sciences University)

- Peer-review system can sometimes restrict the development of innovative ideas into research. Thus the development of consortia as the fetal and neonatal consortium should allow opportunities to conduct high risk innovative research
- Encourage the development of trans-national research programs in fetal and neonatal health
- Restructuring of research funding is not unique to Canada and is occurring in many countries including US, UK, Germany, Australia, New Zealand.
- Unique opportunity to shape the future of health research in Canada
- Symbiotic development of population health and basic biomedical science as evident by the approach to investigating fetal origins of adult diseases
- Good health outcomes drive increased government funding and vice versa
- Be prepared to conduct research in the future in the constantly changing global technology advancements
- Encourage major investment in research training programs for both basic science and clinical research
- Develop clinical research networks
- Funding for research training to allow students and fellows to be able to develop research expertise in the best possible environment anywhere in the world
- To provide competitive career awards for clinical trainees to accommodate for long term training periods
- Avoid institutional parochialism in research in CIHR
- Be proud to be a perinatal scientist

DIRECTIONS FOR THE POST-WORKSHOP CONSORTIUM

- Consensus was achieved for the continuation of a strong Fetal-Neonatal Research Consortium which is associated primarily with one CIHR Institute, with participation in several other Institutes. It is anticipated that there will be an Institute dedicated towards reproduction, development, maternal, child, youth and family health, which will be the logical home base for this consortium.

Principles and functions for ongoing activities of the Fetal-Neonatal Research Consortium:

1. Maintain international links
 - To lobby for joint funding programs with a single review process
 - To establish linkages with national funding agencies from other partner countries such as the NIH, Wellcome Trust, etc., and professional organizations such as the Royal Colleges
 - To establish an Advisory Board with international representation
2. Interact with other existing and future consortia. The possible linkages include the Canadian Neonatal and Paediatric Nutrition Network, Reproduction and Development, Canadian Perinatal Programs Partnerships, Building Capacity for Health in Families, Canadian Paediatric and Obstetric Clinical Trials Network, Canadian Clinical Pharmacology Network.
3. Maintain strong links among research groups within the consortium
 - To be flexible in interactions among the disease based and organ based research groups
 - To develop strategies for enhancing interactions between the cross-cutting research themes
4. Expand the membership of the consortium to include possible underrepresented cross-cutting research themes, e.g. clinical trials, health services research, genetics, informatics, developmental biology, bioethics
5. Establish effective communication links among the consortium members and partners
 - To establish and maintain a web site. A potential web site is available for the consortium through the web site www.perinet.org maintained at Queen's University.
 - To publish a periodic newsletter
 - To widely disseminate the report of this workshop
6. Maintain and enhance already established links with governmental and non-governmental organizations, and identify and establish links with additional governmental and non-governmental organizations.
7. Identify potential strategic initiatives or request for applications (RFAs) for incorporation within one or more CIHR Institutes where the consortium membership will have high likelihood of successful funding.
 - To develop and advocate for these initiatives in a timely fashion, so that they will be sufficiently prepared for submission for consideration when the CIHR Institutes are established.

8. Ensure that the proposed increase in the CIHR budget will be realized to enhance fetal-neonatal research.
 - To effectively lobby with politicians and general public with regards to the importance and relevance of fetal-neonatal research
9. Advise and inform the governing council of CIHR on possible structures and governance of consortia.
10. Advocate for strong representation from the fetal-neonatal consortium at the levels of the scientific director and the institute advisory board of the primary CIHR Institute of affiliation:
 - To lobby for strategic initiatives that are relevant to this consortium
 - To develop appropriate resources which will enable the activities of this consortium
11. Establish an administrative structure and a business plan for the consortium in order to achieve the objectives in both short and long terms
 - To establish a steering committee
 - To determine how best to develop a financial base from the current resources
 - To identify and seek additional sources of funding
 - To establish a secretariat to coordinate the activities of the membership and steering committee as well as to simplify linkages among the members
12. Disseminate information obtained through the consortium activities to the public, the governing council of the CIHR, government, partners etc.
13. Advise the Governing Council of CIHR regarding the establishment of appropriate peer review committees which include the necessary research expertise to adequately review the interdisciplinary research proposals
14. Develop strategies to provide optimal opportunities for trainees
 - To establish new funding mechanisms for bridging from completion of training to junior faculty positions
 - To create opportunities for training in interdisciplinary and multidisciplinary research in state-of-the art laboratories
 - To develop effective mentorship programs to encourage and support existing and prospective trainees in fetal and neonatal research
 - To develop workshops similar to the NIH Aspen Training Program related to grant writing, peer-review system, manuscript writing
 - To provide networking opportunities
 - To ensure trainee representation on the Institute Advisory Boards
 - To develop mechanisms for career counseling

National Fetal-Neonatal Symposium Workshop Report

Executive Summary

1. The first National Fetal-Neonatal Symposium Workshop was held in Banff, Alberta, January 14-16, 2000 attended by 89 delegates including 5 international advisors and 5 graduate trainees.
2. The Workshop objectives were to bring together individuals from all CIHR sectors with interests in fetal-neonatal health; identify current national strengths; identify and outline new opportunities for interaction and areas of research; recognize and promote national and international collaboration; establish new and innovative training programs to graduate students and postdoctoral (MD, PhD) trainees that recognize national needs, strength and excellence.
3. The discussion focussed around opportunities in 6 areas of current national strength: perinatal brain development and injury; cardiovascular development; fetal growth and development; the lung-perinatal respiratory system; the placenta in fetal-neonatal health and disease; preterm labour.
4. The Consortium was a resounding success, and established new partnerships and identified new research directions.
5. Activities of the Consortium should be developed in the following areas:-
 - promote and build national and international linkages
 - expand membership to include under-represented cross-cutting themes
 - build associations with government agencies, NGO's, professional groups, lay organizations
 - establish a communication network within the Consortium
 - identify strategies to develop requests for application (RFA's) in strategic areas identified by the Consortium
 - promote fetal-neonatal health research within CIHR and CIHR institutes
 - act as an advocate on key levels and committees within CIHR, and build liaison groups
 - establish an administrative structure and business plan for the Consortium
 - establish a communications strategy to lay organizations, health professionals and the lay public around the activities of the Consortium
 - develop strategies to provide optimal opportunities for trainees
6. The Consortium should assist and promote applications to CIHR through IHRT and related mechanisms.
7. The Organizing/Advisory group of the Consortium should meet as soon as the CIHR institute structure was announced to identify key alignments.
8. The support of MRC/CIHR, AHFMR, Health Canada, and research institutes and organizations concerned with fetal-neonatal and women's health was gratefully acknowledged. The Workshop allowed attainment of a new horizon and recognition of new opportunities in Canada that would not otherwise have been possible.

The Fetal-Neonatal Research Consortium

Workshop

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PerkinElmer Wallac

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