



CPSP

CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM



2007 RESULTS



Canadian
Paediatric
Society



Public Health
Agency of Canada

Agence de la santé
publique du Canada



Mission Statement

To contribute to the improvement of the health of children and youth in Canada by national surveillance and research into childhood disorders that are high in disability, morbidity, mortality and economic costs to society, despite their low frequency.

Study to improve understanding of juvenile arthritis in Canada



CANADIAN PEDIATRIC SOCIETY
CPS
société canadienne de pédiatrie

I juvenile idiopathic arthritis is chronic, often debilitating childhood illness. While estimates suggest that first to five years over 100,000 children in Canada suffer from this disease, there is national consensus Canada lacks the resources, funding and research to understand paediatric rheumatism. Program, which is headed by the Public Health Agency of Canada, will be the first to generate data on the whole country.

"This study is an exciting opportunity to see what's out there," said Dr. Laine Parent, a rheumatologist at BC Children's Hospital and one of the study's principal investigators. "Many parents have tried to determine the cause of their child's illness, but almost all have been down the rheumatology

specialty routes, which don't lead us to the whole picture. We recognize that rheumatologists are specialists in adult diseases, so we're going to look at things that aren't seen in the first step toward identifying causes."

The study, which began in October, will build on work underway by the Canadian Pediatric Rheumatology Group to establish paediatric rheumatologic centres across the country. Work done through the CPSD will play an important part in identifying current gaps in care, particularly in rural parts of the country.

"While this is just the first step it isn't just about collecting data, it's about making a direct investment in care for our patients," said Dr. Parent. "We're excited, thinking that we can do something better than what we've done before."

On List Serve

places because of it."

For study details, contact Louise Parentland, Secretary of Coordination, at lparent@cps.ca or visit www.cps.ca and follow the links to CPSD &



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Acknowledgements

The key strength of the Canadian Paediatric Surveillance Program (CPSP) is its commitment to the improvement of the health of children and youth in Canada and around the world. This would not be possible without the participation of Canadian paediatricians, subspecialists and other health care providers in the monthly collection of information on rare paediatric conditions, principal investigators who design studies and analyze the data to provide knowledge and educational solutions, and the guidance of the Steering Committee members. We thank them all.

We also thank IMPACT (Immunization Monitoring Program ACTIVE) centres for their role in the verification of data collected and for their support of the CPSP.

We gratefully acknowledge the financial support received to maintain and expand the program. A summary of supporters is found on page 10 in this report.

The strong partnership between the Canadian Paediatric Society (CPS) and the Public Health Agency of Canada (PHAC) allows the program to grow in Canada and to take a leadership role on the international scene.

Foreword

Federal Minister of Health

As Canada's Minister of Health, I am pleased to congratulate the Canadian Paediatric Society for the successful completion of the twelfth annual report of the Canadian Paediatric Surveillance Program (CPSP). By monitoring and increasing awareness of rare childhood diseases and public health issues, the CPSP is contributing to a healthier future for Canadian children.

The CPSP is an important program for surveillance, research and policy development related to the health of children and youth. Much of the program's success can be attributed to the valuable contributions and support of a large, national network of dedicated paediatricians. I commend the efforts of everyone involved.

Highly regarded throughout the international community, the program extends beyond Canada's borders to inform internationally on children's health and provide a model for similar monitoring programs in countries around the world.

The Government of Canada looks forward to a continued partnership with the Canadian Paediatric Society and its members, the provinces and territories, and other stakeholders to improve the overall health and well-being of Canadian children. Together, we can make a difference.



The Honourable
Tony Clement

Chief Public Health Officer of Canada

I am pleased to introduce the twelfth annual report of the Canadian Paediatric Surveillance Program (CPSP), a collaborative program of the Canadian Paediatric Society and the Public Health Agency of Canada. Highly regarded by the scientific community, the data produced by this program is helping to shape and establish public health policy and programs. I commend the Canadian Paediatric Society on its success.

The CPSP was created to collect vital information and to increase our knowledge on childhood diseases. Over the years, the CPSP has established a robust surveillance system and collaborative research network both in Canada and abroad. The Public Health Agency of Canada is pleased to partner with the CPSP in pursuing our common goal of improving the health of children and youth in Canada.

As Chief Public Health Officer, I would like to take this opportunity to thank all the paediatricians who contribute to the CPSP. Your time and dedication is crucial to the success of this program, and to advancing the health and well-being of children and youth across the country.



Dr. David
Butler-Jones

President of the Canadian Paediatric Society

This year, the CPSP conducted 13 different studies and has planned six more for the coming year. This is a great ongoing accomplishment, and special thanks should be given to Danielle Grenier, CPSP Medical Advisor, and Gilles Delage, Chair of the Steering Committee for the last six years. Gilles is stepping down now after helping steer us through an external review whose outcome was glowing and a renewal of our crucial relationship with the Public Health Agency of Canada.

This collaborative national research network is completely dependent on our researchers and all the participants. For particular studies, essential partners have been the Paediatric Demyelinating Disease Network, coroners and pathologists, endocrinologists, geneticists and rheumatologists. The International Network of Paediatric Surveillance Units, of which we are a founding member, is becoming an increasingly important means of collaboration.

We thank all our participants in this research that sheds such important insight on a range of less common conditions that affect the lives of many children and youth.



Dr. Gary Pেকেles

CPSP Chairman

As outgoing Chair, I would like to attest to some of the great contributions to paediatric research that the CPSP has achieved:

- confirming a Canada free of poliomyelitis and variant Creutzfeldt-Jakob disease;
- reaffirming the importance of vitamin K and vitamin D in the prevention of hemorrhagic disease of the newborn and vitamin D deficiency rickets, respectively;
- alerting to the risks of wheeled baby walkers, infant bath seats, lap-belt syndrome and magnetic toys;
- documenting the increasing cases of type 2 diabetes mellitus associated with obesity and overweight in the paediatric population.

These studies illustrate the importance of national paediatric epidemiological research to advance medical knowledge and to inform on public health decisions.

Thanks to all the participants and contributors. The CPSP is a well-established program in the research community, nationally and internationally. Long live the CPSP!



Dr. Gilles Delage

CPSP Steering Committee

Dr. Gilles Delage (Chair)	Canadian Paediatric Society
Dr. Laura Arbour	Canadian College of Medical Geneticists (Liaison)
Dr. Garth Bruce	Canadian Paediatric Society
Ms. Marie Adèle Davis	Canadian Paediatric Society
Dr. Kimberly Dow	Paediatric Chairs of Canada
Dr. Kevin Gordon	Canadian Association of Child Neurology (Liaison)
Dr. Danielle Grenier	Canadian Paediatric Society
Dr. Bryce Larke	Canadian Paediatric Society
Dr. Catherine McCourt	Centre for Health Promotion, Public Health Agency of Canada
Mr. Paul Muirhead	Consultant
Ms. Louise Painchaud	Canadian Paediatric Society
Dr. Jeff Scott	Council of Chief Medical Officers of Health (Liaison)
Ms. Anne-Marie Ugnat	Centre for Health Promotion, Public Health Agency of Canada
Dr. Wendy Vaudry	IMPACT (Immunization Monitoring Program ACTive) (Liaison)
Dr. Lynne Warda	Canadian Paediatric Society
Dr. Sandra Woods	Canadian Paediatric Society
Dr. Lonnie Zwaigenbaum	Canadian Paediatric Society

CPSP Working Group

Ms. Marie Adèle Davis	Canadian Paediatric Society
Ms. Laurence Gillieson	Canadian Paediatric Society
Dr. Danielle Grenier	Canadian Paediatric Society
Ms. Louise Painchaud (Chair)	Canadian Paediatric Society
Ms. Anne-Marie Ugnat	Centre for Health Promotion, Public Health Agency of Canada

Publications 2003-2007

Published papers related to studies

(See www.cps.ca/cpsp for a complete list of abstracts with hotlinks.)

Epidemiology and outcome of necrotizing fasciitis in children: An active surveillance study of the Canadian Paediatric Surveillance Program. Ihuoma E, Davies HD. *J Pediatr* 2007;151(7):79-84

Active surveillance: An essential tool in safeguarding the health and well-being of children and youth (Commentary). Grenier D. *CMAJ* 2007;177(7):169-71

Vitamin D-deficiency rickets among children in Canada. Ward LM, Gaboury I, Ladhani M, Zlotkin S. *CMAJ* 2007;177(7):161-6

Beyond counting cases – Public health impacts of national paediatric surveillance units. Grenier D, Elliott EJ, Zuryski Y, Pereira RR, Preece M, Lynn R, von Kries R, Zimmerman H, Dickson NP, Virella D. *Arch Dis Child*; Published Online First: 11 December 2006. doi:10.1136/adc.2006.097451

Incidence and causes of severe neonatal hyperbilirubinemia in Canada. Sgro M, Campbell D, Shah V. *CMAJ* 2006;175 (6):587-90

Neonatal herpes simplex virus infection in Canada: Results of a three-year national prospective study. Kropp RY, Wong T, Cormier L, Ringrose A, Burton S, Embree JE, Steben M. *Pediatrics* 2006;117:1955-62

Population-based study of incidence and risk factors for cerebral edema in paediatric diabetic ketoacidosis. Lawrence SE, Cummings EA, Gaboury I, Daneman D. *J Pediatr* 2005;146:688-92

An epidemiological analysis of CHARGE syndrome: Preliminary results from a Canadian study. Issekutz KA, Graham JM, Prasad C, Smith IM, Blake KD. *Am J Med Gen* 2005;133A:309-17

Behavioural profile and symptoms of autism in CHARGE syndrome: Preliminary Canadian epidemiological data. Smith IM, Nichols SL, Issekutz KA, Blake KD. *Am J Med Gen* 2005; 133A:248-56

Subacute sclerosing panencephalitis: Results of the Canadian Paediatric Surveillance Program and review of the literature. Campbell C, Levin S, Humphreys P, Walop W, Brannan R. *BMC Pediatrics* 2005;5:47

Prospective surveillance of Canadian children with the haemolytic uraemic syndrome. Proulx F, Sockett P. *Pediatr Nephrol* 2005;20:786-90

Neonatal herpes simplex virus infections in Canada. Kropp RY, Wong T, Burton S, Embree J, Steben M. *Int J STD AIDS: Clin Pract Sex Health* 2004;15(S1):2

Incidence of Smith-Lemli-Opitz syndrome in Canada: Results of three-year population surveillance. Nowaczyk MJM, Wayne JS, Zeesman S, Douketis JD. *J Pediatr* 2004;145(4):530-5

Canadian Paediatric Surveillance Program evaluation: An excellent report card. Grenier D, Doherty J, MacDonald D, Scott J, Delage G, Medaglia A, Davis MA. *Paediatr Child Health* 2004;9(6):379-384

Surveillance for progressive intellectual and neurological deterioration in the Canadian paediatric population. Keene DL, Sutcliffe T, Harman P, Grenier D. *Can J Neurol Sci* 2004;31(2):220-4

Canadian Paediatric Surveillance Program confirms low incidence of hemorrhagic disease of the newborn in Canada. McMillan DD, Grenier D, Medaglia A. *Paediatr Child Health* 2004;9(4):235-8

Canadian Paediatric Surveillance Program: A developmental check-up. Scott J. *Paediatr Child Health* 2004;9(1):13-4

Paediatric adverse drug reactions can be fatal. Grenier D, Doherty J, Medaglia A. *Paediatr Child Health* 2003;8(4):218

Highlights published in 2007 in *Paediatrics & Child Health*

(See www.cps.ca/cpsp for a complete list of highlights with hotlinks.)

Canadian Paediatric Surveillance Program Quiz. *Paediatr Child Health* 2007;12(10):841,866

A simple pneumonia... or not? *Paediatr Child Health* 2007;12(9):780

Poliomyelitis – Are Canadians still at risk? *Paediatr Child Health* 2007;12(8):708

Call for new studies: Research opportunities. *Paediatr Child Health* 2007;12(7):611

Transdermal contraceptive patch: Safe or risky treatment? *Paediatr Child Health* 2007;12(6):505

The changing landscape of diabetes in Canadian children. *Paediatr Child Health* 2007;12(5):400

First episode of acute demyelination of the central nervous system: Should I worry? *Paediatr Child Health* 2007;12(4):337

Severe immune-mediated adverse drug reactions and previous history of drug allergy. *Paediatr Child Health* 2007;12(3):224

Congenital rubella syndrome: Preventing missed opportunities. *Paediatr Child Health* 2007;12(2):142

Booster seat use: Better safe than sorry! *Paediatr Child Health* 2007;12(1):64

Presentations in 2007

(See www.cps.ca/cpsp for a complete list of presentations with hotlinks.)

National

Clinically isolated demyelinating syndromes of the central nervous system in Canadian children. Banwell B, Kennedy J, Bar-Or A, Sadovnick D, Arnold D, and the Pediatric Demyelinating Disease Network, Banff, in December.

Type 2 diabetes in children and youth. Dean H. Family Medicine Forum, Winnipeg, in November.

International comparison of severe neonatal hyperbilirubinemia and herpes simplex virus infection. Grenier D, Sgro M, Wong T, Manning D, Tookey P, Jones CA. Canadian Paediatric Society Annual Conference, Montreal, in June.

Diagnosis and management of multiple sclerosis and related disorders in children. Royal College of Physicians and Surgeons of Canada Lecture. Banwell B. Canadian Paediatric Society Annual Conference, Montreal, in June.

The changing landscape of diabetes in Canadian children. Amed S, Dean H. CPSP concurrent session, Canadian Paediatric Society Annual Conference, Montreal, in June.

Poster – National surveillance of non-type 1 diabetes (NT1DM) in Canadian Children. Amed S, Dean H, Hamilton J and the NT1DM study team. Canadian Paediatric Society Annual Conference, Montreal, in June.

National surveillance for non-type 1 diabetes in Canadian children. Amed S, Dean H, Hamilton J and the NT1DM study team. Canadian Association for Health Services and Policy Research Annual Meeting, Toronto, in June.

Poster – Risk factors for type 2 diabetes in youth with medication induced diabetes. Amed S, Dean H, Hamilton J and the NT1DM study team. Canadian Paediatric Society Annual Conference, Montreal, in June.

Congenital myotonic dystrophy in the US National Registry of myotonic dystrophy. Prendergast P, Magalhaes S, Campbell C. Annual Congress of the Canadian Neurological Sciences Federation, Edmonton, in June.

International

Poster – Impact of surveillance on injury prevention: The Canadian experience. Grenier D, Ugnat A-M, Painchaud L. Annual Meeting of the European Society for Paediatric Research (ESPR), Prague, in October.

Poster – International comparison of severe neonatal hyperbilirubinemia and herpes simplex virus infection. Grenier D, Sgro M, Manning D, Wong T, Jones CA. Annual Meeting of the European Society for Paediatric Research (ESPR), Prague, in October.

Incidence and cohort study of congenital DM. Campbell C, Siu V, Venance S, Jacob P. International Myotonic Dystrophy Consortium IDMC-6, Milan, in September.

Poster – Risk factors for type 2 diabetes in youth with medication induced diabetes. Amed S, Dean H, Hamilton J and the NT1DM study team. The Pediatric Academic Societies/Society for Pediatric Research (APS/SPR) Annual Meeting, Toronto, in May.

Poster – International comparison of severe neonatal hyperbilirubinemia and herpes simplex virus infection. Grenier D, Sgro M, Manning D, Wong T, Jones CA, Tookey P. The Pediatric Academic Societies/Society for Pediatric Research (APS/SPR) Annual Meeting, Toronto, in May.

Indigenous health research through surveillance. Grenier D, Ugnat A-M, Painchaud L. International Meeting on Indigenous Child Health: Solutions, Not Problems, Montreal, in April.

L'impact de la surveillance sur la prévention des blessures : L'expérience canadienne. Grenier D, Ugnat A-M, Painchaud L. Association des pédiatres de langue française (APLF) meeting, Marrakesh, in April.

Funding



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The CPSP is a collaborative program of the Canadian Paediatric Society and the Public Health Agency of Canada.

We gratefully acknowledge the following organizations that have provided funding to the CPSP during part or all of 2007.

Non-governmental sources

- Abbott Laboratories Ltd.
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- Children's Health Research Institute (Children's Hospital of Western Ontario)
- Children's Hospital of Eastern Ontario
- Children's Optimal Therapeutics Program, Children's Health Research Institute
- Complementary and Alternative Research and Education Program
- Hema-Quebec
- The Hospital for Sick Children
- IWK Health Centre – Dalhousie University
- Janeway Children's Hospital Foundation
- Lawson Health Research Institute
- Manitoba Institute of Child Health
- Multiple Sclerosis Scientific Research Foundation
- Ontario Federation for Cerebral Palsy
- Ontario Neurotrauma Foundation Prevention Committee
- William Singeris National Centre for Myotonic Dystrophy Research

Surveillance at Work

Overview

The importance of surveillance to the practice of medicine cannot be overstated. Through the ongoing, systematic collection of data, the burden of disease can be determined, interventions to prevent the occurrence of a disorder can be assessed, and information collected can be used in the development of health policy. Surveillance takes research data into action.

The CPSP provides an innovative means to undertake paediatric surveillance and increase awareness of childhood disorders that are high in disability, morbidity, mortality and economic cost to society, despite their low frequency. Preference is given to studies that have strong public health importance or could not be undertaken any other way. All studies in the program must conform to high standards of scientific rigour and practicality and the CPSP assures the confidentiality of all information collected. To enhance data capture on individual studies, the program works collaboratively with other professional groups, such as family physicians, psychiatrists, pathologists/coroners, and adult endocrinologists. The program also offers an opportunity for international collaboration with other paediatric surveillance units worldwide.

Process

The CPSP Steering Committee oversees the program and reviews new study proposals. Upon initiation of a new study, practising Canadian paediatricians, paediatric subspecialists and other health care providers receive a summary of the protocol, including the case definition and a brief description of the condition. This serves to educate and increase awareness of conditions under surveillance while providing a uniform basis for reporting. The CPSP uses a two-tiered reporting process to ascertain and investigate cases: an initial 'check-off' form and a detailed questionnaire. The full process is summarized in Figure 1 and includes the 3Ds of surveillance: detection, deduction and dissemination.



Reporting

The 'check-off' form, listing the conditions currently under surveillance, is mailed monthly to participants. For each condition, respondents are asked to indicate the number of new cases seen in the last month, including 'nil' reports. A 'nil' report is very important in active surveillance; the CPSP cannot simply assume that no reply means no cases.

Participants report all cases meeting the case definitions, including suspect or probable cases. This sometimes leads to duplicate reports but avoids missed cases. Case ascertainment is monitored and verified by investigating duplicate reports and comparing data with relative programs or centres.

Confidentiality is maintained by using only non-nominal patient information, such as the date of birth, sex of the child and comments on the condition. This anonymous information is used to exclude duplicates and is sent to the original respondent to request case-specific information. Once the detailed questionnaire is returned to

the CPSP, it is forwarded to the investigator for analysis. The investigator is responsible for contacting the respondent if further information is required to confirm or exclude a case.

TABLE 1

**Initial response rates (%)
and number of participants for 2007**

Provinces/territories	Reporting rates (%)	Number of participants
Alberta	83	290
British Columbia	80	266
Manitoba	81	124
New Brunswick	85	31
Newfoundland and Labrador	87	48
Nova Scotia	87	100
Northwest Territories	100	3
Nunavut	100	1
Ontario	81	994
Prince Edward Island	95	8
Quebec	77	663
Saskatchewan	68	54
Yukon	100	3
Canada	80	2,585

TABLE 2

**2007 detailed questionnaire completion rates
as of May 1, 2008**

Studies/conditions	Reported cases	Pending	% Completion rate
Acquired demyelinating syndromes of the central nervous system	29	1	97
Acute flaccid paralysis	94	7	93
Acute rheumatic fever	8	0	100
Adverse drug reactions – serious and life-threatening	45	0	100
Congenital cytomegalovirus infection	34	3	91
Congenital myotonic dystrophy	24	1	96
Head injury secondary to suspected child maltreatment (abuse or neglect)	145	12	92
Juvenile idiopathic arthritis	133	14	89
Kernicterus	16	1	94
Medium-chain acyl-coenzyme A dehydrogenase deficiency	28	2	93
Non-type 1 diabetes mellitus	217	12	94
Severe combined immunodeficiency	20	2	90
Transfusion-related acute lung injury	1	0	100
Total number of cases (all studies)	794	55	93

Participants who do not reply every month receive quarterly reminders. In addition, information on the monthly compliance rates and the number of cases reported is mailed quarterly to all participants to keep them informed of progress. The CPSP is encouraged by the 80% national reporting rate (Table 1) and the 93% response rate for completion of detailed questionnaires (see Table 2 for study breakdown).

Participant workload

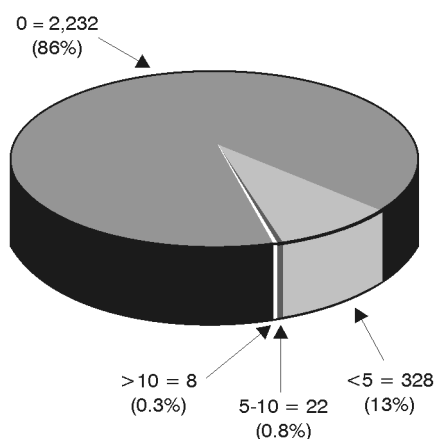
The monthly reporting system is simple and the follow-up study questionnaires are easy to complete. As only non-nominal, non-identifiable data are collected through the CPSP, respondents do not hesitate to provide clinical information.

In 2007, the majority of participants (86%) had ‘nil’ cases to report. The importance of zero reporting must be re-emphasized. Figure 2 illustrates the number of cases reported by respondents in 2007. As studies come and go, the workload shifts to different subspecialties. The 2007 studies with the most reports were non-type 1 diabetes mellitus and head injury secondary to suspected child maltreatment (abuse or neglect).

The CPSP is extremely grateful that the majority of participants faithfully complete the detailed questionnaires subsequent to reporting cases. This demonstrates that they appreciate the enormous value of the scientific data collected and reinforces

FIGURE 2

**Number of cases reported
by respondents in 2007**



the Steering Committee's insistence on short, precise and pertinent detailed questionnaires.

To thank paediatricians and paediatric subspecialists for their tremendous commitment and support, 1,779 personal certificates were sent to acknowledge CPSP participation in 2007, and 262 letters of thanks went to participants who reported a case in 2007. In addition, Drs. Sarah Barker (ON) and Keith Gregoire (ON) were selected in this year's early-bird draw, each winning a dinner for two. The lucky winners of the year-end draws for complimentary registration for the June 2008 CPS Annual Conference in Victoria, BC, were Dr. Nibhas C. De (ON), who responded for all months in 2007, and Dr. Nancy Gagné (QC), who completed and returned two questionnaires for reported cases.

Investigators' corner

The CPSP provides investigators, through its timely, active surveillance system, an innovative means of obtaining non-nominal, national data on low-frequency diseases and conditions from approximately 2,590 participants. The program is committed to a case ascertainment rate of over 90% and, due to follow-up reminders to non-responders, obtains a response rate of 93% on detailed questionnaires (Table 2). The CPSP offers an opportunity for international collaboration with other paediatric surveillance units worldwide and a chance to make a difference in the health and wellbeing of Canadian children and youth.

Individual researchers are encouraged to submit proposals for new studies that meet the *Criteria considered for inclusion of studies* outlined in Table 3 and follow the *Format for submission* detailed in Table 4. The Steering Committee reviews submissions at its spring and fall meetings, giving preference to studies that have either strong scientific and public health importance or those that could not be undertaken any other way. Following the review, studies must receive ethical approval and have external funding arrangements in place before final acceptance to the program. Researchers interested in obtaining more information about the program are encouraged to visit the website at www.cps.ca/cpsp or contact the CPSP senior coordinator at cpsp@cps.ca.

One-time survey questions

The CPSP is also available to investigators as a cost-effective tool to survey participants on a one-time basis in order to identify the prevalence of a problem or to answer a specific question. Once approved by the CPSP Steering Committee, the one-time survey question is sent to all participants with the monthly initial reporting form. Collected results are forwarded to the investigator for data analysis.

Results of the 2007 one-time survey question on magnetic toys are found on page 56.

TABLE 3

Criteria considered for inclusion of studies

Rarity	Disorders of such low incidence or prevalence that national ascertainment of cases is needed (less than 1,000 cases a year)
Public health importance	Clearly addressing a public or paediatric health issue
Scientific importance	Demonstrated scientific interest and importance
Uniqueness	Proposal must demonstrate a clear need for data on a condition or disorder for which there is only limited information and for which surveillance is the most appropriate means of collecting the data
Quality of proposal	Proposal must state clear and achievable objectives, practicability, patient confidentiality, adequate resources, clear questionnaire and method of evaluation
Workload of paediatricians	Steering Committee must be convinced that reporting will not make excessive additional demands on the workload of paediatricians
Priority will be given to diseases that are not currently notifiable or, if notifiable, have sufficient indication of under-notification. Investigators are expected to demonstrate that potential funding is available.	

TABLE 4

Format for submission

Proposals for new studies should include:
<ul style="list-style-type: none"> • Name of principal investigator • Names of co-investigators • Brief abstract of proposal • Proposed starting date and duration • Specific study objectives • Statement of justification, including expected scientific and public health impacts • Case definition • Expected number of cases • Plan for ethical review • Funding arrangements • Identification of projected date for completion of analysis

Glossary of terms for tables of cases in each study results

Reported: Reports of cases received; Duplicates: Cases reported by more than one person; Excluded: Cases not meeting the case definition; Pending: Detailed reports not received or not yet confirmed; Confirmed: Cases verified as meeting the case definition.

Studies timeline

TABLE 5

CPSP studies timeline (by end date)

Study	Start date	End date	Total confirmed cases to December 31, 2007
Group B strep	January 1996	December 1996	178
Neural tube defects	January 1997	December 1998	107
Creutzfeldt-Jakob disease	January 1997	June 1999	1
Hemorrhagic disease of the newborn	January 1997	December 2000	6
Subacute sclerosing panencephalitis	January 1997	December 2000	3
Cerebral edema in diabetic ketoacidosis	July 1999	June 2001	23
Progressive intellectual and neurological deterioration	July 1999	June 2001	59
Anaphylaxis	January 2000	June 2001	732
Hemolytic uremic syndrome	April 2000	March 2002	140
Smith-Lemli-Opitz syndrome	January 2000	December 2002	35
Hepatitis C virus infection	February 2001	January 2003	58
Neonatal liver failure/perinatal hemochromatosis	February 2001	January 2003	10
Necrotizing fasciitis	September 2001	August 2003	37
Neonatal herpes simplex virus infection	October 2000	September 2003	58
Neonatal hyperbilirubinemia – severe	July 2002	June 2004	258
Vitamin D deficiency rickets	July 2002	June 2004	69
CHARGE association/syndrome	September 2001	August 2004	90
Congenital rubella syndrome	January 1996	December 2004	9
Prader-Willi syndrome	January 2003	December 2004	31
Early-onset eating disorders	March 2003	February 2005	160
Lap-belt syndrome	September 2003	August 2005	28
Osteogenesis imperfecta	January 2004	December 2005	27
Acquired demyelinating syndromes of the central nervous system	April 2004	March 2007	221
Acute rheumatic fever	April 2004	March 2007	68
Congenital cytomegalovirus infection	March 2005	February 2008	46
Head injury secondary to suspected child maltreatment (abuse or neglect)	March 2005	February 2008	169
Non-type 1 diabetes mellitus	April 2006	March 2008	284
Medium-chain acyl-coenzyme A dehydrogenase deficiency	September 2005	August 2008	26
Transfusion-related acute lung injury	September 2005	August 2008	3
Acute flaccid paralysis	January 1996	December 2008	535
Adverse drug reactions – serious and life-threatening	January 2004	December 2008	157
Kernicterus	January 2007	December 2008	10
Severe combined immunodeficiency	April 2004	March 2009	21
Juvenile idiopathic arthritis	October 2007	September 2009	117
Congenital myotonic dystrophy	March 2005	February 2010	20

Survey questions

TABLE 6

CPSP survey questions

Injuries associated with baby walkers	January 2002
Lap-belt syndrome	February 2003
Acquired demyelinating syndromes of the central nervous system (CNS)	February 2004
Infant bath seats	June 2004
Acute flaccid paralysis	November 2004
Congenital cytomegalovirus infection	January 2005
International adoption	September 2005
Adolescent depression and side effects of selective serotonin reuptake inhibitors (SSRI)	November 2005
Adverse events associated with paediatric complementary and alternative medicine	January 2006
Magnetic toys	August 2007

CPSP Principal Investigators



Surveillance studies in 2007



Dr. Brenda Banwell
Acquired demyelinating
syndromes of the central
nervous system



Jeannette Macey
Acute flaccid paralysis



Dr. Christina Templeton
Acute rheumatic fever



Margaret Zimmerman
Adverse drug
reactions – serious
and life-threatening



Dr. Wendy Vaudry
Congenital
cytomegalovirus
infection



Dr. Craig Campbell
Congenital myotonic
dystrophy



Dr. Susan Bennett
Head injury secondary to
suspected child maltreatment
(abuse or neglect)



Dr. Lori Tucker
Juvenile idiopathic
arthritis



Dr. Michael Sgro
Kernicterus



Dr. Chitra Prasad
Medium-chain acyl-coenzyme A
dehydrogenase deficiency



Dr. Shazhan Amed
Non-type 1 diabetes
mellitus



Dr. Ezzat Farzad
Severe combined
immunodeficiency



Dr. France Gauvin
Transfusion-related
acute lung injury

Surveillance Studies in 2007



Acquired demyelinating syndromes of the central nervous system

April 2004 to March 2007 (final report)

Highlights

- The study confirmed 221 incident cases of demyelination from April 1, 2004 to March 31, 2007.
- Of the confirmed cases, 210 (95%) children underwent a brain MRI and 181 (82%) required treatment.
- During the study period, communication with families regarding the potential diagnosis of MS increased significantly, from 65% in year one to 83% by year three.

Background

Acquired demyelinating syndromes (ADS) of the central nervous system (CNS) in childhood are serious events and may not be as rare as previously thought. The varied clinical phenotypes of initial acute CNS demyelination, termed clinically isolated syndromes (CIS), include optic neuritis, transverse myelitis, hemisensory or hemimotor syndromes, cerebellar or brainstem dysfunction, alone (monosymptomatic CIS), in combination (polysymptomatic CIS), or associated with encephalopathy (acute disseminated encephalomyelitis, ADEM). Advancing the understanding of demyelination in children is of the utmost importance given that these children may suffer significant acute and long-term morbidity, and are at risk for recurrent demyelination characterizing the chronic autoimmune disease multiple sclerosis (MS).

This study gathered case-specific data to document the clinical features, epidemiological characteristics, familial autoimmune profile, and current medical care practices provided to children with ADS. This initiative provided a measure of the impact of CNS demyelination on Canadian children, and enhanced clinical care of affected children by increasing awareness among Canadian paediatricians of CNS demyelination, and of MS in particular, facilitating prompt and specialized care for children with this disease.

Objectives

- 1) Increase awareness and understanding of paediatric CIS and MS among Canadian paediatricians.
- 2) Define the incidence of the various forms of paediatric CIS in Canadian children.
- 3) Evaluate the epidemiological features and familial autoimmune profile of children with CIS.
- 4) Describe current treatments offered to children with CIS across Canada, with attention to differences in treatment protocols across regions and between community and tertiary care facilities.
- 5) Evaluate paediatric and paediatric neurologist practices in discussing with families the possibility of MS following CIS in childhood.

Case definition

Children less than 18 years of age with one of the following syndromes are reported:

- Acute loss of vision (**optic neuritis**): decreased visual acuity of one or both eyes, typically maximal over a period of days, often associated with pain. CT/MRI may show swelling and abnormal signal of optic nerves.
- Spinal cord dysfunction (**transverse myelitis**): weakness and/or numbness of both legs +/- arms, often associated with bladder retention



- with maximal deficits four to 21 days after symptom onset. MRI may demonstrate swelling and/or abnormal signal in the spinal cord.
- Acute neurological deficits: **acute neurological dysfunction** (i.e., weakness, numbness/tingling, loss of balance, impaired eye movements, double vision, poor coordination) maximal within four to 21 days after onset associated with MRI evidence of at least one area of abnormal white matter signal of the brain or spinal cord. Level of consciousness should be normal, and fever or neck stiffness absent.
 - Acute disseminated encephalomyelitis (**ADEM**): acute neurological deficits (weakness, numbness, loss of balance) associated with at least two of the following: 1) viral prodromal illness within the last 28 days, 2) fever, 3) stiff neck, 4) headache, 5) altered level of consciousness or behaviour, or 6) seizures. MRI shows multiple areas of abnormal signal in the white matter.

Exclusion criteria

- Demyelination of the peripheral nervous system (i.e., Guillain-Barré syndrome, chronic inflammatory demyelinating polyneuropathy)
- Leukodystrophies (i.e., metachromatic leukodystrophy, adrenoleukodystrophy, etc.) or mitochondrial disease
- Active CNS infection (i.e., bacterial meningitis, herpes simplex encephalitis, Lyme disease, HIV, HTLV-1, West Nile virus)
- Radiation/chemotherapy-associated white matter damage

Results

Demographic and incidence data

There were 307 reports of possible demyelination received between April 1, 2004 and March 31, 2007. Of these reports, 221 met the inclusion criteria, eight cases are pending review (detailed questionnaire not received), and 46 were duplicate reports. Thirty-two cases did not meet eligibility criteria: 17 cases were reported but already had clinically definite MS, seven had alternative diagnoses and eight had demyelinating events outside the surveillance period.

TABLE 7

Acquired demyelinating syndromes of the central nervous system cases from April 1, 2004 to March 31, 2007

Reported	Duplicates	Excluded	Pending	Confirmed
307	46	32	8	221

Of the 221 confirmed cases, the majority were from Ontario (47%), followed by Quebec (15%), Alberta (12%), British Columbia (10%), Manitoba (6%) and Prince Edward Island (5%). Four other provinces accounted for the remaining confirmed ADS cases.

The mean age of confirmed ADS cases is 10.5 years (range 0.7–18.0 years) and the female to male ratio is 1.1:1 (116 females, 105 males).

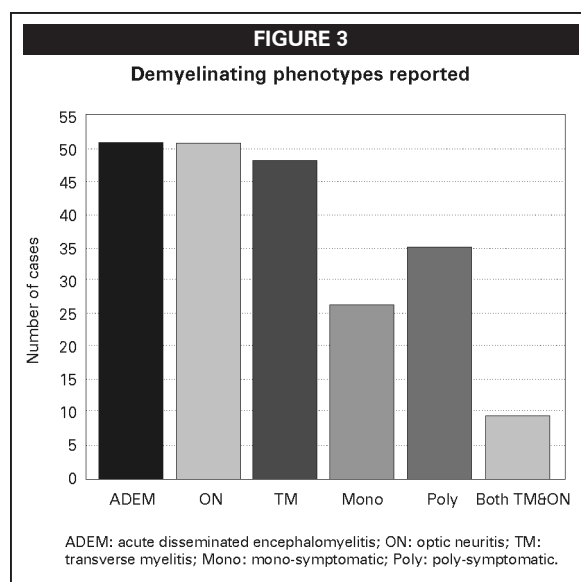
Epidemiological and familial autoimmune data

Most of the children reported (195/221) were born in Canada. The majority of patients reported European ancestry (57%). Other ancestries included Asian (10%), Central and South American (6%), Middle Eastern (3%), Caribbean (2%) and mixed ancestry (10%). Ancestry was not recorded in 17 patients. Seventeen of the confirmed cases (7.7%) reported a family history of MS.

Clinical features and paediatric practices

Figure 3 illustrates the various clinical phenotypes seen with the reported cases of acute demyelination. The majority of ADS cases were ADEM (n=51) and optic neuritis (n=51), followed by transverse myelitis (n=48), poly-symptomatic presentation (n=35), mono-symptomatic presentation (n=27) or both transverse myelitis and optic neuritis (n=9). Of the 51 optic neuritis cases, 21 were documented as bilateral and 30 were unilateral.

Brain MRIs were performed in 210 cases (95%); abnormal white matter changes were reported for 173 cases (78%). Treatment with corticosteroids or immune globulin for the demyelinating event was required for the majority of patients (82%). Ninety-three percent (93%) of the confirmed cases were first-time acute demyelinating syndromes, and the risk of recurrent demyelination was discussed with the patients and families in 83% of these patients.



Conclusion

Based on annual estimates from members of the Paediatric Demyelinating Disease Network (PDDN), it is estimated that 107 children will present with acute demyelination each year in paediatric centres across Canada. The study's data approach this number, when averaged over three years, and results indicate that the incidence is nearly 74 cases per year. The difference could be from an overestimation of expected cases or under-reporting in some provinces.

The distribution of cases reported in each province has remained fairly consistent over the duration of the study.

The majority of children with ADS required treatment for their demyelinating event and 95% children underwent brain MRI imaging over the course of the study. The proportion of children undergoing MRI has remained high (87% in 2004, 100% in 2005, 91% in 2006 and 100% in 2007). This demonstrates continued understanding and awareness of MRI as a diagnostic tool in demyelination.

For all children with acute demyelination of the central nervous system, a risk exists for recurrent demyelination (MS). The data indicate that this risk is being discussed with at least 83% of patients and families, which will likely translate to more rapid diagnoses of MS in affected children.

Principal investigator

- Brenda Banwell, MD, Paediatric Multiple Sclerosis Clinic, The Hospital for Sick Children, 555 University Ave, Toronto ON M5G 1X8; tel.: 416-813-7857; fax: 416-813-6334; e-mail: brenda.banwell@sickkids.ca (representing the Paediatric Demyelinating Disease Network, which includes 23 paediatric care facilities across Canada)

Acute flaccid paralysis

January 1996 to December 2008

Highlights

- Canada's AFP surveillance performs below World Health Organization targets for AFP detection, stool specimen collection and follow-up for residual paralysis.
- High duplicate reporting rates suggest good sensitivity in monitoring.
- Poliovirus infection has to be ruled out for each AFP case, ensuring that potential import or import-associated cases are rapidly detected and managed.
- Detection of a wild poliovirus case in Australia in 2007 serves as a reminder that polioviruses are circulating elsewhere in the world.

Background

Elimination of indigenous wild poliovirus transmission was certified in Canada, and the rest of the Americas, in September 1994. However, until global eradication of poliomyelitis is achieved, there remains an ongoing risk for importation of wild polioviruses. Outbreaks of polio are occurring in four endemic and several newly re-infected regions in Africa and Asia (www.polioeradication.org). Over 1,300 cases were reported worldwide in 2007. Consequently, active surveillance with appropriate follow-up investigation of acute flaccid paralysis (AFP) in children less than 15 years of age continues to be used to monitor for potential cases of paralytic poliomyelitis. This important activity is Canada's safeguard in maintaining vigilance for potential import or import-associated cases of paralytic poliomyelitis.

Sensitive monitoring and detection of AFP cases are important in order to ensure that appropriate investigations are promptly conducted to rule out polio. As well, documentation of AFP monitoring and investigation activities is the means by which Canada is able maintain its polio-free certification status.

The expected background annual incidence for AFP in the absence of wild poliovirus transmission is one AFP case per 100,000 of the population aged less than 15 years. This equates to approximately 60 cases per year in Canada. AFP surveillance is conducted jointly through two paediatric

surveillance networks in Canada: the IMPACT (Immunization Monitoring Program, ACTIVE) network of paediatric tertiary care centres, which initiated AFP surveillance in 1991; and the CPSP, which implemented case detection and documentation in 1996. This report presents the combined results of Canada's AFP surveillance in 2007.

Objectives

The overall goal of AFP surveillance is to monitor Canada's polio-free status by ensuring sensitive, active surveillance and prompt, appropriate investigation of AFP cases to rule out the possibility of poliovirus infection. Key objectives, based on World Health Organization (WHO) quality assurance criteria include:

- 1) Ability to detect at least one case of non-polio AFP (including Guillain-Barré syndrome [GBS]) per year for every 100,000 children less than 15 years of age.
- 2) Collection of adequate stool specimens for poliovirus examination from at least 80% of AFP cases within 14 days of the onset of paralysis.
- 3) Completion of follow-up exams at least 60 days after paralysis onset to verify the presence of residual paralysis in at least 80% of AFP cases.

Case definition

Acute onset of focal weakness or paralysis characterized as flaccid (reduced tone) without other obvious cause (e.g., trauma) in children less

than 15 years of age. Transient weakness (e.g., post-ictal weakness) should not be reported.

Results/discussion

TABLE 8

Acute flaccid paralysis cases in 2007

Reported	Duplicates	Excluded	Pending	Confirmed
94	42	9	7	36

There were 94 reports of AFP with onset in 2007, including 36 confirmed cases (Table 8). The majority of reports (83%) were submitted by the CPSP, with the remainder originating from IMPACT. Approximately one-third (30%) of the detailed questionnaires were submitted from IMPACT hospitals. Nearly half of the confirmed cases (47%) were reported by Ontario and Quebec.

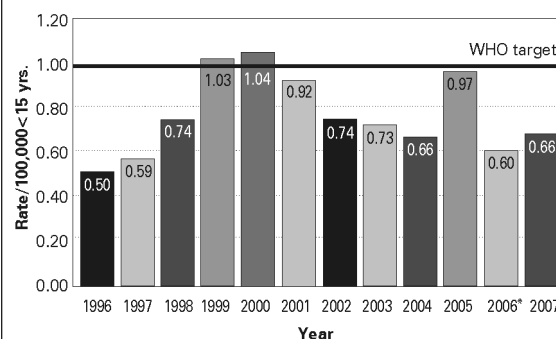
Nine reports were excluded: eight based on age criteria (children aged 15 years or older) and the other based on a confirmed diagnosis of infantile botulism, eliminating the need to rule out polio. The 36 confirmed cases in 2007 represent a non-polio AFP detection rate of 0.66/100,000 children under 15 years of age. This is below the 1/100,000 per year expected rate. However, the number of cases captured more than once by the CPSP and IMPACT was high, with an average of two reports for each confirmed case. The annual AFP incidence rate may be artificially low due to delays in receiving detailed questionnaires, seven of which are still pending (Figure 4).

In 2007, AFP cases ranged in age from six days to 14 years (median 6.1 years, mean 7.4 years). As in previous years, cases were fairly evenly distributed across the age groups. There were 1.2 male cases for every female case reported.

Only 15 (42%) AFP cases had details of routine childhood immunization history. Of these, 12 had received age-appropriate polio immunization with inactivated poliovirus vaccine (IPV). An additional seven cases reported polio vaccination information as “up-to-date” but had no accompanying vaccine or date details. One case was born outside Canada or travelled abroad and had documented vaccination with a combination of OPV and IPV doses.

FIGURE 4

Non-polio AFP detection rate, Canada 1996-2007



* Includes seven delayed reports not included in the CPSP 2006 Results

Importance of stool investigation:

A stool specimen collected within two weeks of the onset of paralysis for isolation of wild or vaccine strain poliovirus is the single most important laboratory investigation for **all** AFP cases to confirm or to rule out a diagnosis of paralytic poliomyelitis.

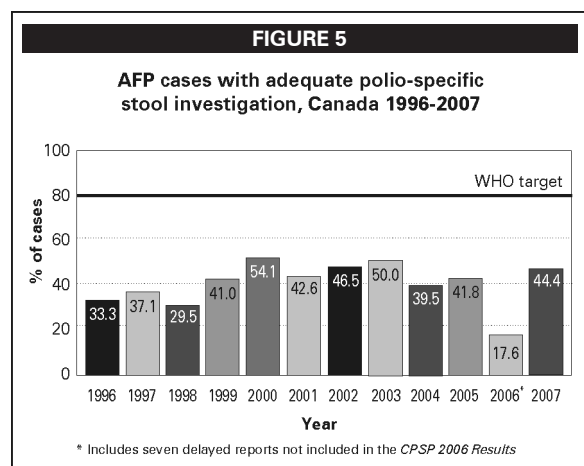
Specimens should be collected within two weeks after the onset of paralysis. Although sensitivity of virus isolation decreases thereafter, specimens collected up to six weeks after onset of paralysis may yield virus.

Examination of paired serum samples for evidence of a four-fold or greater rise in poliovirus antibody titre and/or the presence of poliovirus-specific IgM antibody in a single serological specimen further enhance the evaluation of cases.

Investigation for polio virus, other enteroviruses or *Campylobacter*

Virological investigation included collecting and testing stool specimens for 18 cases (50%), cerebrospinal fluid for 20 cases (55%), throat swabs for 10 cases (27%) and polio-specific serology for two cases (4%). Where stool was collected, 16 cases (44%) had adequate investigation for isolation of poliovirus within two weeks of the onset of paralysis. In the remaining two cases, stool collection was later, when the sensitivity of virus isolation was decreased. Rates of adequate stool investigation were consistently below the WHO surveillance target of 80% (Figure 5). While there was no positive identification of polioviruses from any of the virological investigations, aetiology was identified for three cases: botulism, cytomegalovirus, and Lyme disease. In another (Bickerstaff brainstem encephalitis), *Bartonella henselae* and arbovirus antibody were reported findings. In 2007, as in previous years, a low number of cases (12) were investigated for

Campylobacter infection, and no tests to date have been positive.



Neurological investigations

In 2007, approximately 75% of cases underwent at least one type of neurological investigation (CSF examination, nerve conduction studies/electromyography, MRI/CT scan), with all three types conducted equally often. CSF chemistry showed abnormalities in 20/28 cases (71%). Electromyography and/or nerve conduction studies showed abnormalities in 21/27 cases (78%). MRI or CT scans showed abnormalities in 14/27 cases (52%).

As observed in previous years, the majority of AFP cases (n= 27, 75%) were diagnosed as GBS, two of which were Miller-Fisher variant. In 2006

and 2007, the transverse myelitis (TM) diagnoses are lower than in previous years. In 2007, the six “other” diagnoses (Table 9) included acute motor neuropathy (2), Bell’s Palsy (1), Bickerstaff brainstem encephalitis (1), infantile botulism (1) and spinal amyotrophy (1).

Hospitalization and outcome

All but one of the AFP cases (97%) in 2007 required hospitalization, with lengths of stay ranging from one to 90 days (average 17 days). Outcome at the time of the initial report was documented for 34 cases (94%): three cases (9%) fully recovered, 25 cases (74%) partially recovered with residual weakness or paralysis, and five cases (15%) not recovered but condition reported as progressing. Only 14 cases (42%) had reported status at 60 days, including four cases who had fully recovered, eight with partial recovery/some residual weakness or paralysis, and two with outcomes pending. This is below the 80% WHO-recommended target for high quality AFP surveillance and may be affected by the timing of report completion/submission.

Conclusion

The 36 confirmed AFP cases is less than expected, and Canada’s non-polio AFP detection rate of 0.66/100,000 remains below the WHO target of 1/100,000. This target has been met only twice (in 1999 and 2000) since AFP surveillance began in 1996, despite seemingly sensitive surveillance and the detection of confirmed cases through both the CPSP and IMPACT networks. Canada’s

TABLE 9

Neurological diagnosis of AFP cases, Canada

Diagnosis	Number of cases											
	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006*	2007
Polio	0	0	0	0	0	0	0	0	0	0	0	0
Guillain-Barré syndrome	21	29	34	50	49	42	33	33	27	36	29	27
Transverse myelitis	6	2	6	7	4	8	7	4	7	10	3	3
Other†	2	3	1	4	8	4	3	7	4	9	2	6
Not specified or undetermined	1	1	3	—	—	—	—	—	—	—	—	—
Total	30	35	44	61	61	54	43	44	38	55	34	36

* Includes seven delayed reports not included in the CPSP 2006 Results

† Other: encephalitis/encephalomyelitis/encephalopathy, myelopathy, radiculopathy/radiculoneuritis, plexitis/lumbosacral plexitis, brachial neuritis, rhombomyelitis; also included in 2005: botulism, diffuse hypotonicity, acute areflexia, and acute disseminated encephalomyelitis (ADEM)

lower than expected AFP rates may be a result of under-detection of cases combined with delayed reporting, or it may be a true reflection of lower baseline levels for non-polio AFP in Canada and other developed countries.

The vast majority of reported AFP cases continue to undergo one or more neurological investigations. Given that most AFP cases are diagnosed as either GBS or TM, clinical signs and symptoms consistent with these conditions may favour neurological investigations. However, polio-specific laboratory investigations remain vital for WHO-recommended evaluation and documentation of all cases, including those in which poliomyelitis is not being considered as a possible diagnosis.

The quality of AFP surveillance could be improved through increased stool sampling and virological testing for polioviruses and non-polio enteroviruses, better documentation of 60-day follow-up with observation of any residual paralysis, and timely completion and submission of case reports and detailed questionnaires. These improvements are essential in order to comply with the International Health Regulations. The Regulations provide the legal framework for coordinating international efforts to contain health emergencies and prevent the spread of listed diseases like poliomyelitis. All countries must be ready to comply by 2012.

Global polio eradication initiative

Despite some continuing challenges, global polio eradication was reaffirmed by the Advisory Committee on Polio Eradication (Geneva, 2005) and at the World Health Assembly (Geneva, 2006). While just over 1,300 cases of poliomyelitis were reported globally in 2007, 92% of these occurred in four countries where indigenous polio transmission is still occurring: Nigeria, India, Pakistan and Afghanistan. Importantly, 2007 vaccination campaigns used monovalent oral

polio vaccine and had the lowest-ever-reported incidence of type 1 poliovirus.

For polio-free countries, Australia's July 2007 detection of a case of wild type poliomyelitis in a 22-year-old student returning from a visit to Pakistan was a wake-up call, particularly for industrialized nations where indigenous poliovirus circulation has long since been eradicated. The risk of disease importation is real and all countries must remain vigilant to rapidly detect and respond to possible imported cases. The Pan American Health Organization cautions that countries in the Americas may not be prepared to adequately respond to a poliovirus importation if they are not conducting adequate and timely stool investigation to definitively rule out poliovirus infection in **all** AFP cases less than 15 years of age (and AFP *in any age* that could be due to poliovirus infection). All countries, including Canada, must maintain high quality AFP surveillance and high vaccine coverage.

Principal investigator

- Jeannette Macey, A/Head of Disease Surveillance, Centre for Immunization and Respiratory Infectious Diseases, Infectious Disease and Emergency Preparedness (IDEP) Branch, Public Health Agency of Canada, 130 Colonnade Rd, PL6502A, Ottawa ON K1A 0K9; tel.: 613-946-0486; fax: 613-952-8053; e-mail: Jeannette_Macey@phac-aspc.gc.ca

Co-investigator

- Tammy Lipskie, Public Health Agency of Canada

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Acute rheumatic fever

April 2004 to March 2007 (final report)

Highlights

- Acute rheumatic fever is extremely rare in the Canadian paediatric population, with an estimated incidence of 2.9 per million population per year.
- The most common major manifestation was carditis, in 59% of cases.
- Significant morbidity included arthritis and chorea in 54% and 38% of cases, respectively.
- Medical treatment was required in all confirmed cases, often with multiple medications.

Background

Acute rheumatic fever is a post-infectious collagen vascular disease affecting the heart, joints and central nervous system. It follows untreated Group A streptococcal (GAS) pharyngitis after a latent period of approximately three weeks. It does not occur after other GAS infection, such as skin infection (impetigo). Worldwide, it remains the most common cause of acquired heart disease in children, but the incidence is widely variable from region to region, with the vast majority of cases now occurring in developing countries.

The incidence of acute rheumatic fever in developed countries has decreased dramatically since its last peak in the 1970s, but it has not disappeared, and remains an important public health issue. The reason for its decrease is not fully understood. The decline in incidence in the early 20th century had already begun prior to the introduction of effective antimicrobial agents, but common use of penicillin to treat symptomatic sore throat may have contributed to the decline somewhat. Socioeconomic factors such as overcrowding and low income are known to be significant risk factors. The majority of cases of rheumatic fever follow cases of pharyngitis due to specific M serotypes of GAS, most commonly 1, 3, 5, 6, 18, 19 and 24. Spontaneous fluctuation of the prevalence of these serotypes is known to occur.

Rheumatic fever is not a reportable condition in Canada, and in the current era of evidence-based, judicious use of antibiotics, ongoing surveillance of this now rare but serious condition is crucial. Rheumatic heart disease

is a life-long complication of the condition, which can lead to ongoing medical and surgical needs and can interfere with employment, causing significant socioeconomic impact. However, the risk of developing rheumatic fever must be balanced against the risk of encouraging microbial antibiotic resistance, which is a growing problem in all developed nations and carries its own impact.

There is no current Canadian literature to suggest incidence. This is a sufficiently rare condition; only a national reporting system could gather statistically significant numbers.

Objectives

- 1) Determine the incidence of rheumatic fever among Canadian children.
- 2) Determine the relationship between modern rheumatic fever and demographic features, such as overcrowding and low household income.
- 3) Describe current Canadian treatment practices.
- 4) Determine the morbidity and mortality of first episode rheumatic fever in Canada.

Case definition

Report any child up to and including 18 years of age who meets the most recent modification of the Jones criteria for diagnosis of an initial attack of rheumatic fever (Table 10).

The definition of carditis will require clinical evidence of cardiac involvement in the form of a pathological murmur, pericarditis or congestive heart failure. Current literature is divided as to whether silent echocardiographic findings should

be included; the questionnaire will include this information, but the case definition will remain faithful to current international consensus requiring clinical manifestations.

TABLE 10

Guidelines for the diagnosis of initial attack of rheumatic fever, Jones criteria

Major manifestations	Minor manifestations
Carditis Polyarthritides Chorea Erythema marginatum Subcutaneous nodule	Clinical Arthralgia Fever Laboratory findings Increased acute phase Reactants: - Increased erythrocyte sedimentation rate - Increased C-reactive protein - Prolonged P-R interval
All cases, except Sydenham's chorea, will require documentation of antecedent group A streptococcal infection either by positive throat culture, rapid antigen test or an elevated or rising antibody titre. Antistreptolysin O titre measurement is the preferred test because it is able to distinguish recent streptococcal infection from chronic pharyngeal carriage.	
If there is evidence of recent streptococcal infection, the presence of two major manifestations or one major and two minor manifestations will be considered diagnostic.	

Results

TABLE 11

**Acute rheumatic fever cases
April 1, 2004 to March 31, 2007**

Year	Reported	Duplicates	Excluded	Pending	Confirmed
2004	47	18	6	0	23
2005	39	12	5	0	22
2006	39	18	4	0	17
2007	8	1	1	0	6
Total	133	49	16	0	68

The acute rheumatic fever study ran from April 1, 2004 to March 31, 2007. All preliminary reports have now been accounted for. There was a high rate (72%) of duplication of reports, primarily because patients were seen by more than one specialist or subspecialist within the group of reporting paediatricians.

Demographic data

The mean age at diagnosis was 10 years (range 3 to 17 years) and the gender balance was even,

with a female-to-male ratio of 1:1 (34 females, 34 males). Over half (57%) of patients lived in urban households. Very few lived with large numbers of people in the household; only 4.4% of patients came from families with more than six people in the household.

The distribution of cases among provinces was as follows: 23 cases from Ontario, 15 from Quebec, 11 from Manitoba, nine from Alberta and the remaining 10 cases from three provinces (BC, NS and NL).

Systems affected

The most common major manifestation was carditis, with 40 (58.8%) patients affected. Of those, 35 had mitral valve disease, 23 had aortic disease and 18 had both. Smaller numbers had right-sided valve involvement and pericarditis (eight and six, respectively).

Arthritis occurred in 37 (54%) patients. The most frequently affected joints were, in order, ankles, knees, wrists, elbows and fingers. The arthritis was migratory in 71.7% of cases and affected five or more joints in 37.8%.

Twenty-six (38%) children experienced chorea. Of these, 92% had purposeless movement, 69% had emotional lability, 50% had personality change and 31% had motor weakness.

The least-often reported major manifestations were erythema marginatum and subcutaneous nodules, with only six and four children being affected, respectively.

Current treatment

Medical treatment was needed in all confirmed cases. Antibiotics were given in 84% of cases to eradicate streptococcal infection, prior to starting prophylaxis. Almost all cases (97%) received long-term prophylaxis, primarily orally using penicillin (n=51) or erythromycin (n=2) in the presence of a penicillin allergy, and a significant minority (n=10) receiving monthly IM injections of benzathine penicillin.

Anti-inflammatory medications were required in 52 (76.5%) children, with the most common agents being naproxen, aspirin and prednisone. Three children were given intravenous immunoglobulin (IVIG) infusions.

Chorea was most often treated with valproic acid. Alternatives included haloperidol and benzodiazepines.

Of the 40 cases with carditis, 23 required medical therapy. Enalapril and other after-load reducing agents were given in 18 cases. Two children required inotropic support. Valve surgery was performed on two patients during the study period, and it was planned in two other cases.

Conclusion

The completed three-year surveillance study for first onset acute rheumatic fever in Canada has indeed shown that this is a very rare disease at present. The total 68 confirmed cases of ARF gives an estimated incidence of 2.9 (3.64) cases per million population per year, based on the 2006 Census data of 7,814,600 children aged 0-19 years, from Statistics Canada (www40.statcan.ca/101/cst01/demo10a.htm).

There was no mortality within the study period, but morbidity was high, particularly with the 58.8% incidence of carditis, which can be a lifelong complication.

All patients required some form of medical therapy for their disease; in many cases, more than one medication was used. Two patients required cardiac

surgery for valve disease and for two others it was being planned at the time of reporting.

There are no current published data on the incidence of rheumatic fever in the Canadian paediatric population, other than this surveillance study. It is hoped that this knowledge, combined with studies into evolving bacterial resistance, will ultimately guide practice in the treatment of pharyngitis, keeping the risks balanced to provide evidence-based care for patients.

Principal investigator

- Christina G. Templeton, MD, Janeway Children's Health and Rehabilitation Centre, 300 Prince Philip Dr, St. John's NL A1B 3V6; tel.: 709-777-4462; fax: 709-777-4747; e-mail: christina.templeton@hccsj.nl.ca

Co-investigators

- Austin R. Cooper, MD, Janeway Children's Health and Rehabilitation Centre
- Paul Dancey, MD, Janeway Children's Health and Rehabilitation Centre
- Derek G. Human, BM, University of British Columbia
- Proton Rahman, MD, Memorial University of Newfoundland

Adverse drug reactions – serious and life-threatening

January 2004 to December 2008

Highlights

- In 2007, the CPSP confirmed 41 cases of suspected paediatric adverse reactions.
- Product groups most commonly associated with suspected adverse reactions were anti-infective agents, followed by anticonvulsants and anti-neoplastic agents.

Background

Adverse drug reactions (ADRs) rank as one of the top 10 leading causes of death and illness in the developed world. The direct medical costs of ADRs are estimated to be between US\$30 and 130 billion annually in the United States. These estimates are even more meaningful when compared with other high-cost diseases like diabetes (\$45 billion), obesity (\$70 billion) and cardiovascular diseases (\$199 billion).

Of particular concern is the alarming lack of understanding of ADRs in children. While children are known to be at greater risk than adults, there is a remarkable lack of understanding of causation and therefore a limited ability to avoid or prevent these occurrences. Health-related accreditation bodies estimate that 95% of all ADRs are not reported.

More than 75% of prescribed pharmaceuticals on the market in North America have never been tested in paediatric populations and are used without the benefit of adequate guidelines for safety or efficacy. Clinical practice has focused on adjusting dosage to account for smaller body mass, with the assumption that clinical effects would be equivalent to those observed in adults. It is now understood that a host of biological, developmental and behavioural factors affect the safety and effectiveness of pharmaceuticals when used in paediatric patients. In addition, children often cannot verbally express their own drug therapy experiences. As a result, newborns, infants and children who require medication for acute, chronic and life-threatening diseases are at risk of ADRs, ranging from ineffective treatment and minor ADRs to severe morbidity and death. It is for these reasons that children worldwide are

described as “therapeutic orphans” and are placed at an increased risk of therapeutic failure, while ADRs continue to cause unnecessary disability and death.

Objectives

- 1) To determine the feasibility of an active surveillance system (CPSP) to identify serious and life-threatening paediatric ADRs not currently captured by existing spontaneous reporting systems.
- 2) To identify the products most frequently causing ADRs in children, the type of reactions encountered and the characteristics of those affected.
- 3) To determine the usefulness of the data collected for meaningful analysis and interpretation.

Case definition

Serious and life-threatening adverse drug reactions* in an infant or child up to the age of 18 years, associated with the use of prescription, nonprescription, biological (immunoglobulin) products, complementary medicines (including herbals), and radio-pharmaceutical products.

Report even if you are not certain if the product caused the adverse reaction or you do not have all the reporting details.

Exclusions

Do not report reactions due to medical devices, blood products (platelets, red cells and single-donor plasma), vaccines, poisonings or self-administered overdoses.

* **Noxious and unintended severe** response to a drug, which occurs at any dose and results in emergency observation, hospitalization, persistent or significant disability, or death.

Results

TABLE 12

Adverse drug reaction- serious and life-threatening cases in 2007

Reported	Duplicates	Excluded	Pending	Confirmed
45	0	4	0	41

In 2007, there were 41 confirmed cases of suspected ADRs (Table 12). Of these, 25 were males, 15 were females and one was not determined. Cases ranged from 8 months to 17 years. The majority of reports involved adolescents (n=18), followed by children 6 to 12 years of age (n=16) and then children 5 years and younger (n=9).

The confirmed cases were classified as serious by meeting the following criteria: resulted in a fatal outcome (n=2); were life-threatening (n=9); resulted in hospitalization or prolongation of hospitalization (n=19); or were considered medically important (n=11). A medically important reaction is defined as one that may not be immediately life-threatening or result in death or hospitalization, but that may jeopardize the patient or may require intervention to prevent one of these other outcomes from occurring.

Information regarding patient outcome was provided for all 41 confirmed cases: fatal outcome (n=2); recovered (n=36); and not yet recovered (n=3). The first fatal case involved a pre-adolescent who received clofarabine for the treatment of relapsed acute lymphoblastic leukemia. The patient experienced Stevens Johnson Syndrome, hepatitis with hyperbilirubinemia (>20 times upper limit of normal) and elevated transaminases, and also had pancytopenia. Clofarabine is not marketed in Canada and was obtained for this patient through the Special Access Program. The second case involved an adolescent with cerebral palsy who received succinylcholine for induction of general anaesthesia. The patient experienced a fatal cardiac arrest due to hyperkalemia that was suspected to have been caused by the administration of succinylcholine.

All reports described reactions that were already documented in standard drug reference sources for the health product, except for reactions in three reports: acute renal failure suspected with propolis; Stevens Johnson Syndrome suspected with clofarabine; and disseminated intravascular coagulation suspected with piperacillin-tazobactam and cefotaxime. The information source used for this determination was the Canadian-approved product monograph. When an approved product monograph was not available, the source used was the Compendium of Pharmaceuticals and Specialties (electronic version) or the Micromedex™ Drug Information System.

Suspected health products

Table 13 lists all health products suspected of causing ADRs in the 41 confirmed cases, sorted by the number of reports received for each individual product. In 35 reports, a single product was suspected of causing the reaction(s). Two suspect products used simultaneously were reported in six cases; in one of these six cases, the reporter suspected an interaction between two products. The class of health products most frequently suspected was anti-infective agents (n=12), followed by anticonvulsants (n=9) and anti-neoplastic agents (n=5).

TABLE 13

Suspected or interacting health products (n=47) in ADR cases (n=41) in 2007

Suspected health product	# Reports
Carbamazepine	4
Infliximab, valproic acid	3 each
Atomoxetine, ceftriaxone, cytarabine, minocycline, phenytoin, piperacillin-tazobactam, risperidone, tacrolimus	2 each
Acetaminophen, cephalexin, cefotaxime, clarithromycin, clindamycin, clobazam, clofarabine, fluconazole, ketorolac, moxifloxacin, naproxen, ondansetron, peg-L-asparaginase, propolis, salbutamol, sertraline, sirolimus, succinylcholine, thioguanine, vancomycin, vitamin K1	1 each

Discussion

An initial three-year study evaluating paediatric ADR reports collected through the CPSP was completed at the end of 2006. Active surveillance of paediatric ADR provided important research

data and the study was extended. As in previous years, collaboration with Health Canada continues, and completed ADR reports from the CPSP have continued to be received and processed by the CPSP principal investigator and the Canada Vigilance Program. The Canada Vigilance Program of the Marketed Health Products Directorate, Health Canada, is responsible for collecting and assessing adverse reaction reports for the following health products marketed in Canada: pharmaceuticals, biologics (including fractionated blood products as well as therapeutic and diagnostic vaccines), natural health products and radiopharmaceuticals. The information collected in Canadian adverse reaction reports is entered and maintained in a computerized database and is used to monitor marketed health products. These spontaneous ADR data are sources of information used for detecting potential product-related safety issues and for determining the benefit-risk assessments of these products. The CPSP study will help improve understanding of the scope of ADR problems in the paediatric population and will address public health concerns.

Conclusion

Serious and life-threatening adverse reactions do occur in the paediatric population. The classes

of health products most frequently suspected of causing the adverse reaction(s) are anti-infective agents, followed by anticonvulsants and anti-neoplastic agents. All three classes of health products are frequently used in paediatric care.

The ongoing sharing of safety information through voluntary reporting of ADRs is key to enhancing the benefit-risk profile of health products used in children.

Caveat: Adverse drug reactions (ADRs) to health products are considered to be suspicions, as a definite causal association often cannot be determined. Spontaneous reports of ADRs cannot be used to estimate the incidence of ADRs because ADRs remain under-reported and patient exposure is unknown.

Principal investigator

- Margaret Zimmerman, BSc, Manager, Patient Safety Section, Therapeutic Effectiveness and Policy Bureau, Marketed Health Products Directorate, Health Canada, Tunney's Pasture, Building 7, AL 0701C, Ottawa ON K1A 0K9; tel.: 613-957-2806; fax: 613-948-7996; e-mail: margaret_zimmerman@hc-sc.gc.ca

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Congenital cytomegalovirus infection

March 2005 to February 2008

Highlights

- The study confirmed nine cases of congenital CMV in 2007.
- Infants were often severely affected and diagnosed prenatally by fetal ultrasound or maternal serology.
- All reported infants were diagnosed by viral isolation or molecular diagnostics.

Background

Congenital cytomegalovirus infection (CMV) is the most common congenital infection, affecting from 0.2% to 2.4% of all live births. Approximately 10% of infected infants manifest significant clinical illness in the newborn period with a variety of manifestations including poor growth, microcephaly, jaundice, hepatosplenomegaly, anemia and thrombocytopenia. Almost all of these infants will go on to have later neurologic sequelae. Even if asymptomatic at birth, approximately 5–17% will have neurodevelopmental abnormalities, including sensorineural hearing loss, which may only become apparent in infancy or later in childhood. Congenital CMV infection is a difficult diagnosis to prove retrospectively, as definite diagnosis requires isolation of the virus from the newborn in the first three weeks of life. Diagnosis beyond that age may indicate acquired infection from exposure to the virus in the birth canal or breast milk. This infection has devastating consequences and is of great public health significance.

Active surveillance for congenital CMV infection is timely, as the following intervention strategies are on the horizon:

- The National Institutes of Health (NIH) have recommended universal newborn hearing screening for early diagnosis and intervention to improve outcomes in congenital deafness.
- Ganciclovir therapy in neonates with neurological manifestations of congenital CMV infection improves hearing outcome.
- CMV vaccines are currently being developed. This would allow for primary prevention in CMV-susceptible women, similar to the congenital rubella vaccine success story.

Surveillance of congenital CMV infection through the CPSP will help public health policy-makers to plan their intervention strategies on a national sampling of the paediatric population.

Objectives

- 1) Determine the number of congenital CMV infections recognized by Canadian paediatricians.
- 2) Determine the reason for initiating CMV testing in newborns.
- 3) Describe clinical manifestations and risk factors of infected infants in the newborn period.
- 4) Obtain detailed epidemiological data, including maternal histories, on confirmed cases.
- 5) Describe the virologic method of diagnosis and the current usage of antiviral therapy.

Case definition

Report all newborns with CMV infection confirmed in the first three weeks of life by any of the following laboratory methods:

- Culture of CMV from an appropriate clinical specimen*
- Polymerase chain reaction (PCR) positive for CMV from an appropriate clinical specimen*
- Presence of CMV-specific IgM in the neonatal or cord blood†

* An appropriate clinical specimen is urine, throat, blood, CSF or tissue biopsy.

† Serology (i.e., TORCH screen) is a very poor way of making the diagnosis. Many newborns with congenital CMV do not produce detectable IgM. Viral isolation or identification is the most reliable diagnostic method.

Results

There were 34 reported cases in 2007: 16 from Ontario, seven from Manitoba and the remaining 11 reports from Quebec and other Western provinces. There were no reports from Eastern Canada. Six duplicate cases were reported; 10 detailed questionnaires are still pending. Of

the 18 completed detailed questionnaires, nine CMV cases were confirmed and nine were excluded, as the diagnostic testing was not adequate – usually because it was not done early enough in life (within the first three weeks) to confirm the presence of congenital CMV infection. This delay in testing can occur either because the diagnosis is not considered in the early neonatal period or because the child was born and initially assessed in a remote centre without immediate access to diagnostic expertise or laboratory testing.

TABLE 14

Congenital cytomegalovirus infection cases in 2007

Reported	Duplicates	Excluded	Pending	Confirmed
34	6	9	10	9

Cumulative results from March 2005 to December 2007

Demographics and epidemiological data

There were 46 confirmed CMV cases out of 116 reports. The majority of reports were from Ontario (n=48), followed by Quebec (n=22), Alberta (n=12), Manitoba (n=11) British Columbia (n=7) and New Brunswick (n=6). The remaining 10 reports were from three provinces (SK, NS and NL). No reports were received from Prince Edward Island or the territories.

Six of the confirmed cases (14%) were from rural areas (population <1,000); four of these rural cases were born to First Nations' women. Maternal ethnicity was as follows: Caucasian (52%), Asian (13%), First Nations (13%), Black (4%), Latin American (2%) and unknown (15%). Of the 46 confirmed cases, 34 of the mothers were born in Canada, six were born outside the country (two immigrated more than five years before, three immigrated between one to five years before) and six were unknown. Mothers (n=39) had a mean age of 24.5 years (range 16–41 years) and 28 were primiparous.

Clinical presentation

Twenty-eight (61%) of the congenitally infected infants presented prenatally: three by maternal serology, indicating primary infection, and 25 by fetal imaging showing either IUGR or cranial

abnormalities. The rest of the infants presented in the neonatal period with symptoms ranging from low birth weight (with or without microcephaly) to thrombocytopenia, hepatosplenomegaly, anemia and jaundice. All infants (n=46) were diagnosed with a urine test positive for CMV: 39 by viral culture and 14 by PCR. Newborn IgM serology was positive in only 11 of the infected infants. It was negative in five, not done in 19 and unknown or missing in 11 cases.

Management

Most of the infants had some form of cranial imaging, including head ultrasounds (n=40) (abnormal in 21, normal in 17, done without result in two), cranial MRI or CT scans (n=22) (abnormal in 12, normal in 10). Hearing assessments were carried out on 34 infants (abnormal in nine, normal in 23 and done without result in two). Ophthalmologic assessments were carried out on 37 infants (abnormal in eight, normal in 28 and done without result in one). Of the reported infants, 11 received intravenous ganciclovir therapy. All of these infants had significant neurological symptoms, usually including abnormal cranial imaging. The infected infants remained in the reporting hospital for a combined total of more than 950 days; paediatricians sometimes reported the length of stay at their hospital only, before the infant was transferred to a tertiary care centre. Most infants were admitted to the neonatal intensive care unit for a mean stay of 21 days (n=31, range 0–71 days). One infant was a stillbirth and the four other deaths occurred at 27 days, five weeks, eight weeks, and three months respectively, for an early mortality rate of 11%. The rest were discharged home or transferred to another facility during the reporting period and the final outcomes are not known.

Discussion

Thus far, the surveillance study has confirmed 46 cases of congenital CMV. The current rate of congenital CMV infection in Canada is not yet known. If the rate was 1%, with 10% of these infants being symptomatic in the newborn period, there should be approximately 300 cases per year for the Canadian birth cohort. The relatively

low number of reports may reflect a number of factors: the overall infection rate is probably lower than 1%, but may be that high in certain risk groups; the CPSP may only capture a portion of the diagnosed cases in the country (national laboratory-based surveillance for the same time period will be done if possible to estimate the reporting rate for diagnosed cases); and neonatal symptoms may be subtle and not recognized as congenital CMV early enough in the neonatal period to make a definitive diagnosis. The most accurate measurement of the infection rate will likely have to await population-based surveillance to capture the full spectrum of congenital CMV in Canada. Comparisons of infection rates detected by the CPSP and population-based screening will be important data with which to assess the need for implementation of population-based routine screening for congenital CMV.

More than half of the cases presented prenatally, with most showing abnormal fetal ultrasound (usually of the brain). These infants were severely affected. This emphasizes that infants diagnosed in the neonatal period may represent the “tip of the iceberg”. Less severely affected infants may be missed for diagnostic purposes but still have significant neurological sequelae that remain undiagnosed. Such sequelae, deafness in particular, may be recognized late and intervention subsequently delayed. New Canadian and First Nations’ children appear to be at higher risk of congenital CMV infection; 67% of the infected children born in rural Canada were of First Nations

origin. This observation will await further analysis using data from the complete study.

Viral isolation, or PCR, confirmed the diagnosis from the urine in all cases. Neonatal IgM (as performed by the “TORCH” screen) was performed in a minority of cases and had a low sensitivity. The low rate of serological testing may be a result of the pre-study survey and educational intervention with participants from the CPSP.

Conclusion

Congenital CMV caused significant morbidity during the neonatal reporting period, with affected infants experiencing prolonged hospital stays of high intensity and 24% receiving intravenous ganciclovir therapy. Five infants died, for an early mortality rate of 11%. This early, severe morbidity and mortality likely represents only a small fraction of the true burden of congenital CMV disease in Canada.

Principal investigator

- Wendy Vaudry, MD, Department of Paediatrics, Stollery Children’s Hospital, University of Alberta, Edmonton AB T6G 2R7; tel.: 780-407-1680; fax: 780-407-7136; e-mail: wvaudry@cha.ab.ca

Co-investigators

- Bonita Lee, MD, University of Alberta
- Louise Pelletier, MD, Public Health Agency of Canada
- Rhonda Rosychuk, PhD, University of Alberta

Congenital myotonic dystrophy

March 2005 to February 2010

Highlights

- Eight cases of CMD were confirmed in 2007, in keeping with initial estimates.
- Only one case required prolonged ventilation; life supportive therapy was withdrawn at 27 days due to respiratory failure.
- A very uncommon phenomenon of paternal transmission of CMD was documented in 2007.

Background

Myotonic dystrophy is an autosomal dominant multi-system disorder characterized by muscle weakness and myotonia commonly beginning in adulthood. There are now three genetic loci for the disease but only one of these, DM1, is associated with a congenital form of myotonic dystrophy (CMD). The DM1 mutation is a CTG trinucleotide repeat in the DMPK gene on chromosome 19q13.3. Although the disruption of the DMPK protein may contribute to the symptoms of the disease, the primary pathogenesis is felt to be related to the impact of large accumulations of nuclear mutant mRNA on protein splicing. Myotonic dystrophy demonstrates genetic anticipation, with a more severe phenotype evident at an earlier age in successive generations of affected families. In the case of a child presenting with CMD, the parent who passes the gene defect is almost exclusively the mother. She may have such a mild case as to neither recognize any symptoms nor carry a diagnosis of myotonic dystrophy, making the child the index case for the family.

Although no uniform definition of CMD exists, a genetic diagnosis in baby or mother combined with symptoms of muscle disease early in life are consistent features. During pregnancy, the initial abnormality may include polyhydramnios and premature labour. The diagnosis is made in the newborn period, secondary to respiratory or feeding difficulties. The incidence of CMD has not yet been established through a population-based study and it is unclear how often children are the index cases for their families or how families are using genetic counselling information. Rates of neonatal mortality and morbidity range widely. An

incomplete correlation exists between the number of trinucleotide repeats and symptoms; individuals with larger repeat numbers generally show more severe symptoms. The use of genetic information to predict outcome is difficult due to this variability, and more pragmatic approaches to understanding the prognosis for children with CMD need to be explored.

The current surveillance study is gathering information that will help to clarify some of these issues, and is raising awareness about CMD among Canadian paediatricians. Ultimately, the data obtained about incidence, individual case clinical information and outcomes will help health care providers and families obtain quality information on which to base care management decisions that arise in newborns with CMD.

Objectives

- 1) Determine the incidence and neonatal mortality of CMD in Canada.
- 2) Provide a clear definition of CMD.
- 3) Describe the burden of illness in newborns with CMD, including duration of ventilation and decision to withdraw treatment.
- 4) Identify the relationship between genotype and phenotype in CMD cases.
- 5) Determine the frequency of both the CMD as the index case and the use of genetic counselling services by mothers with CMD.

Case definition

Report any child up to the age of three years with a new diagnosis of CMD. A diagnosis of CMD will be included if children have **both** of the following clinical and genetic criteria:

- Symptoms of myotonic dystrophy in the newborn period (<30 days), such as hypotonia, feeding or respiratory difficulty, requiring hospitalization to a ward or to the neonatal intensive care unit for more than 72 hours;
- CMD genetic tests confirming an expanded trinucleotide (CTG) repeat in the DMPK gene in the child or mother. An expanded CTG repeat size is >200 repeats or E1–E4 classification (E1 = 200–500, E2 = 500–1,000, E3 = 1,000–1,500, E4 > 1,500).

Results/discussion

There were 24 cases reported in 2007. Of these, eight cases met the inclusion criteria and were included as incident cases. The cases have been reported from five different provinces and territories across Canada. Of the eight confirmed cases, five were female and three were male. The children were all diagnosed before they reached one year of age. For one of the confirmed cases, the case report form is not yet available to include in the results; however, some clinical information is available from discussion with the reporting physician. Table 15 demonstrates the number of duplicate cases, those excluded and cases not yet confirmed.

TABLE 15

Congenital myotonic dystrophy cases in 2007

Reported	Duplicates	Excluded	Pending	Confirmed
24	9	6	1	8

One of the eight confirmed CMD cases died while in hospital at 27 days from respiratory failure and withdrawal of life support on this basis. The deceased case had genetic confirmation of CMD with CTG trinucleotide repeats of 1,500.

All eight children had hypotonia, feeding difficulties or respiratory difficulties that led to prolonged hospitalization. The duration of hospital admission ranged from 7 to 45 days. Four (4/7) of the cases required assisted ventilation and three did not. Of these four ventilated children, one died as stated above and the other three living children needed ventilation ranging from 18 hours to

27 days. The children requiring ventilation had trinucleotide repeat expansions ranging from 550 to 1,500. All four ventilated children experienced feeding difficulties. As well, of the four remaining children, two also experienced feeding difficulties, one did not and the fourth child's feeding status is unknown.

Six (6/7) of the children were the index cases for their families. In the final case, the mother had a known diagnosis. The mother did receive genetic counselling, prior to this pregnancy, about the risk of transmission to a child and the phenomenon of genetic anticipation. Surprisingly, in one of the cases, the father was later diagnosed with CDM. This is very rare, with few reported cases of paternal transmission in the literature. The child was mildly affected with only hypotonia in the newborn period; however, the condition was significant enough that the child required observation in the neonatal intermediate care unit for three days and was admitted for seven days in all. The child's CTG expansion was 600–800 and the father's is unknown.

In addition to the surveillance study, an ongoing parallel natural cohort study is available to subjects. In 2007, one child agreed to join the national cohort study, one could not join because of an early death, and in the other six cases agreement to join the cohort is still pending.

In the past year the results of the study were presented at the 2007 Canadian Neuroscience Federation Meeting and at the 6th International Myotonic Dystrophy Consortium. The study has led to collaborative clinical and translational studies with investigators in the U.S. and Canada.

Conclusion

The CMD surveillance confirmed 20 cases in the first 34-month period, which represents slightly fewer cases than the expected 10–12 per year. At the current time, there are two cases under review, one from 2007.

For the complete study period in 2007, the reported children had a wide range of phenotypes, with feeding difficulties being the main cause

of prolonged admission in the newborn period. Prolonged ventilation remains rare, yet continues to be a catalyst for withdrawal of life support at the one month of age period.

Given the variability year to year in the first three-year segment of the study, an extension for an additional two years of surveillance has been granted. Ongoing surveillance over the coming years will be a significant part of drawing more firm conclusions from the study. It is important that CMD be studied, as the impact of this disease is systemic, chronic and often associated with significant morbidity and mortality in the newborn period. A diagnosis of CMD also has wide-ranging implications for families and extended families. The best possible evidence is required to guide parents and health care practitioners in management decision-making.

Principal investigator

- Craig Campbell, MD, Paediatric Neurology, Children's Hospital of Western Ontario, William Singeris National Centre for Myotonic Dystrophy, 800 Commissioners Rd E, London ON N6A 4G5; tel.: 519-685-8332; fax: 519-685-8350; e-mail: craig.campbell@lhsc.on.ca

Co-investigators

- Pierre Jacob, MD, University of Ottawa
- Simon Levin, MD, University of Western Ontario
- Victoria Siu, MD, University of Western Ontario
- Shannon Venance, MD, University of Western Ontario

Head injury secondary to suspected child maltreatment (abuse or neglect)

March 2005 to February 2008

Highlights

- In 2007, the study on head injury secondary to suspected child maltreatment confirmed 75 cases.
- Shaken baby syndrome was the suspected diagnosis in 61% of the cases reported.
- Injuries resulted in 10 deaths; 37% of the confirmed cases had mild-to-severe neurological sequelae.
- Child welfare authorities had previously been involved in 25% of confirmed cases.

Background

Despite the fact that the term “battered child syndrome” was first used in 1962, the study of child maltreatment is still in its infancy in Canada. This is true even though maltreatment comprises a major cause of mortality and morbidity for Canadian children and youth. Even the most basic questions about maltreatment in Canada are just beginning to be answered. There is an incomplete picture of the number of children who suffer abuse or neglect, the extent to which they are harmed, the way health care professionals identify children at risk and the process that is followed to protect those children.

Cases of inflicted head injury, although thankfully reasonably rare, are of great clinical importance, as a large proportion of them result in death or permanent neurological deficits. Internationally, published incidence data of child maltreatment underestimate the extent of the problem, as they differ considerably from actual case studies reported through the legal and/or medical systems. These differences can be attributed to a number of factors, including fear of disclosure (stigma, fear of potential consequences) and failure by professionals to recognize and report child maltreatment. Until recently, the literature regarding the prevalence of child maltreatment was limited, with over 90% of the information originating from the United States and most of the remaining literature coming from the United Kingdom and Australia.

Attempts have been made to quantify the issue in Canada; however, the information is limited. One

effort was a time-limited study examining only shaken baby syndrome and the other was limited to cases where determination of physical harm was made by child welfare workers. As a result, there is much support for tracking these injuries. The *Canadian Joint Statement on Shaken Baby Syndrome* recommends surveillance and collection of data on inflicted head injury.

Objectives

- 1) Describe the incidence of head injury secondary to suspected child maltreatment (abuse or neglect) among Canadian children.
- 2) Describe the incidence of head injury secondary to suspected child maltreatment in at-risk groups among the Canadian paediatric population.
- 3) Identify the presentation, patterns and burden of head injury secondary to suspected child maltreatment.
- 4) Inform strategies to improve protection of children and youth and provide an opportunity to educate health care professionals.

Case definition

Report all new cases of a child up to 14 years of age inclusively, who has any mechanism of head or brain injury consistent with abuse/neglect* (e.g., shaking, impact, suffocation) and that have been reported to provincial/territorial child welfare agencies. Report regardless of whether or not you reported the case yourself to the agency.

The definition of head or brain injury consistent with abuse/neglect includes any objective

diagnostic evidence of head or brain injury. This may include radiologic, ophthalmologic or forensic findings such as skull fracture, cerebral contusion, subdural or epidural or subarachnoid hemorrhage, cerebral edema, retinal hemorrhages, or clinical evidence of a significant head or brain injury (e.g., severe head soft tissue injury, depressed level of consciousness, seizures, focal neurological findings).

* Neglect/failure to protect: the child has suffered harm or the child's safety or development has been endangered as a result of the caregiver(s)' failure to provide for or to protect the child. Please note that the term 'neglect' is not used in some provincial/territorial statutes, but interchangeable concepts include: failure to care and provide or supervise and protect; does not provide, refuses or is unavailable or unable to consent to treatment.

a. Failure to supervise or protect leading to physical harm: the child suffered or is at substantial risk of suffering physical harm because of the caregiver's failure to supervise and protect the child adequately. Failure to protect includes situations in which a child is harmed or endangered as a result of a caregiver's actions (e.g. drunk driving with a child or engaging in dangerous criminal activities with a child).

b. Physical neglect: the child suffered or is at substantial risk of suffering physical harm caused by the caregiver's failure to care and provide for the child adequately. This includes inadequate nutrition/clothing and unhygienic, dangerous living conditions. There must be evidence or suspicion that the caregiver is at least partially responsible for the situation.

Results

Demographic data

Of the 75 cases confirmed to date in 2007, 40% were from the Western provinces (BC, AB, SK and MB), 55% were from Central Canada (ON and QC), 4% were from Eastern Canada (NS and NL) and 1% was from Northern Canada (NWT). The median age at initial presentation was nine months (n=69, range 3 weeks–50 months old). There were 40 boys, 34 girls and the gender of one child was unknown. Of those cases where numbers of children in the household were reported (85%), the median number of children was two (range 1–5 children).

TABLE 16

Head injury secondary to suspected child maltreatment cases in 2007

Reported	Duplicates	Excluded	Pending	Confirmed
145	19	24	27	75

Management

Of the 75 confirmed cases, 62% initially presented to the emergency department, with the remainder

presenting to a family physician or paediatrician. The median number of days between initial and reported presentation was zero (range 0–26). The initial presentation included soft tissue injury (43%), irritability (28%), decreased consciousness (27%), vomiting (23%), seizure (22%), lethargy (19%), apnea (11%) and respiratory difficulty (11%). Of the confirmed cases, 63/75 (84%) were hospitalized. Data on length of stay were available for 54/63 (86%) cases, with a median length of stay of nine days (range 1–150 days). Of the confirmed cases, 34/75 (45%) were admitted to the intensive care unit (ICU). Data on length of stay in the ICU were available for 19/34 of cases admitted to the ICU with a median length of stay of two days (range 1–35 days). A hospital child protection team was involved in 71/75 (95%) of the cases and the police were involved in 59/75 (79%) of the cases. Child welfare authorities had previously been involved in 19/75 cases (25%).

Injuries

Clinical findings were found in all of the 75 cases and included:

- Subdural hematoma (65%)
- Seizures (64%)
- Retinal hemorrhage (53%)
- Skull fractures (51%)
- Bruising (41%)
- Cerebral edema (22%)
- Fractures of long bones or ribs (16%)
- Cerebral contusion (16%)
- Focal neurological findings (13%)
- Subarachnoid hematoma (13%)
- Abrasions (9%)
- Epidural hematoma (6%)
- Abdominal injuries (1%)

Previous medical history was reported for 34 of the cases. The most frequent issues were a premorbid condition, previous maltreatment, excessive crying, prematurity (<36 weeks) and developmental delay. Shaken baby syndrome (SBS) was the suspected diagnosis in 46/75 (61%) of the cases, while other suspected physical abuse accounted for 22/75 (30%) and suspected neglect for 7/75 (9%). Medical status at time of discharge was available for 68 cases. In 10 of these cases (15%) the injuries resulted in death, in 25 cases (37%) there were mild-to-severe neurological sequelae and in 33 cases (48%) the medical status at discharge was normal.

Perpetrator

Perpetrator status was confirmed in 8/75 (11%) of cases, suspected in 31/75 (41%) and unknown in 36/75 (48%). The confirmed or suspected perpetrator was male in 31/39 of the cases where the perpetrator status was confirmed or suspected. Moreover, in 33/39 of the cases the confirmed or suspected perpetrator lived with the child. The relationship to the child of the confirmed or suspected perpetrator was available for all of the 39 cases in which the perpetrator status was confirmed or suspected. In 76% of these cases the confirmed or suspected perpetrator was a parent, and in 9% of cases it was a babysitter. These confirmed or suspected perpetrators had a history of at least one risk factor, with the most common risk factors being domestic violence, few social supports, and drug and alcohol abuse.

Conclusion

Results from the third year of this study have shown that head injury secondary to suspected child maltreatment (abuse or neglect) in children up to 14 years of age inclusively continues to be prevalent in our society, with 75 cases confirmed at a median age of nine months and 46 (61%) of those cases diagnosed as suspected SBS. There was significant mortality and morbidity among confirmed cases. In the 68 cases where the outcome was known at the time of discharge, 10 (15%) resulted in death and 25 (37%) had mild-to-severe neurological sequelae.

These results are consistent with the 2006 results of this study. In 2006, 34 (67%) of the 51 confirmed cases were diagnosed as suspected SBS. Furthermore, in the 45/51 cases where the outcome was known at the time of discharge, three

(7%) resulted in death and 18 (40%) had mild to severe neurological sequelae. Thus, the 2006 and 2007 results show that it is important for all health care providers to keep a high index of suspicion to diagnose affected children.

With as many as 62% of reported cases presenting to an emergency department in 2007, there is a need to adequately educate health care providers in how to identify these cases. The fact that the child welfare authorities had previously been involved in one-quarter (19/75) of cases reinforces the importance of support and close follow-up of at-risk families. Thus far, the findings are consistent and confirm that this study will provide data that can inform educational efforts to support health care professionals in recognizing these cases. This will, ideally, also lead to more effective prevention efforts.

Principal investigator

- Susan Bennett, MB ChB, Children's Hospital of Eastern Ontario, 401 Smyth Rd, Ottawa ON K1H 8L1; e-mail: bennett@cheo.on.ca

Co-investigators

- Tammy Clifford, PhD, Children's Hospital of Eastern Ontario Research Institute
- Gilles Fortin, MD, Sainte-Justine UHC
- Jim King, MD, Children's Hospital of Eastern Ontario
- Morag Mackay, MSc, BScN, European Child Safety Alliance
- Amy Plint, MD, Children's Hospital of Eastern Ontario
- Michelle Ward, MD, Children's Hospital of Eastern Ontario

Juvenile idiopathic arthritis

October 2007 to September 2009

Highlights

- In the first three months of surveillance, 117 cases of newly diagnosed JIA were confirmed.
- The most common JIA subtype is oligoarthritis.
- Two JIA subtypes, enthesitis related arthritis and psoriatic arthritis, frequently not included in studies, are quite commonly seen in this study.
- Joint pain is absent in 10% of patients, a factor often leading to delayed diagnosis.
- To date, children from First Nations appear over-represented amongst children with JIA.

Background

Chronic arthritis in childhood, called juvenile idiopathic arthritis (JIA), is a rare chronic condition of children and adolescents. Although rarely fatal, the condition is long-term and associated with serious physical disability, pain, loss of independence, restrictions in daily activities and social participation, and unemployment as young adults. An increased utilization of health care services has been demonstrated in addition to significant personal and societal costs.

Reliable and accurate data on the scope of chronic arthritis in children and adolescents in Canada are scarce. This information is crucial to determining the health services required by these individuals and in examining the gaps in health service provision. A limited number of epidemiologic studies have tried to measure the scope of JIA in Canada. Annual incidence rates have been reported between 5.3 and 10 per 100,000, and higher point prevalence estimates of 52 per 100,000 in Saskatchewan and 32 per 100,000 in Manitoba have been calculated. However, all these estimates were obtained from paediatric rheumatology specialty centres. Thus, although disease incidence is perceived as relatively low in Canada, there is the distinct possibility of significant underestimation of the number of cases.

A standardized approach to measure the scope and magnitude of JIA in Canada will facilitate development of appropriate interventions that can ultimately lead to improved quality of life for these children.

Objectives

- Ascertain the incidence of JIA in Canada.
- Determine feasibility and usefulness of an active surveillance system of JIA.
- Describe the demographics, including regional and ethnic variations of chronic childhood arthritis in Canada.
- Describe the clinical features of chronic childhood arthritis in Canada at presentation.
- Describe initial management strategies for chronic childhood arthritis in Canada, including treatment choices and referral strategies.
- Generate awareness of this rare disease among paediatric health care professionals.

Case definition

Report any child up to 16 years of age (up to 16th birthday) who presented for the first time with:

- Arthritis: persistent inflammation in one or more joints defined as:
 - ▶ Swelling or effusion, or
 - ▶ Presence of two or more of the following signs:
 - limitation of range of motion
 - tenderness on motion
 - pain on motion
- Duration of disease: \geq six weeks

Exclusion criteria

All other relevant diseases (e.g., infection, malignancy, other systemic inflammatory diseases).

(The case definition is extracted from the definition of the International League of Associations for Rheumatology Classification of Juvenile Idiopathic Arthritis, Petty et al, 2004.)

Results

TABLE 17

**Juvenile idiopathic arthritis cases
October 1 to December 31, 2007**

Reported	Duplicates	Excluded	Pending	Confirmed
124	2	0	5	117

Demographic and epidemiologic data

There were 117 confirmed cases of newly diagnosed JIA in the first three months of active surveillance. The majority of cases were reported from Ontario (35.9%), followed by Alberta (17%), Nova Scotia/P.E.I./Newfoundland/Labrador (14.5%), British Columbia (12%), and Quebec (10.2%). Manitoba and Saskatchewan accounted for the remaining 10.2%. No cases were reported from the territories.

Of the 117 confirmed cases, complete data from the detailed questionnaire are available for 41 patients. The majority of patients (80.4%) were Caucasian, 7.3% were First Nations, 4.9% were Asian, and 4.9% were of mixed ethnicity.

Clinical features at presentation

Joint pain, swelling and morning stiffness were common presenting symptoms, with limp occurring in 68.2% of patients. The median number of affected joints at diagnosis was two (range 0–41). The most commonly affected joints were the knees, followed by the ankles and wrists.

JIA subtypes reported

There are six subtypes of JIA: systemic, oligoarthritis (persistent or extended), polyarthritis rheumatoid factor negative, polyarthritis rheumatoid factor positive, psoriatic arthritis, and enthesitis related arthritis. Patients who do not fulfill criteria in any of these categories, or who fulfill criteria in two or more categories, are considered “unclassified”.

For the 41 patients with complete data, a subtype was assigned in 83% of patients (Table 18). The most common JIA subtype was oligoarthritis. Enthesitis related arthritis was the second most common subtype, followed by polyarthritis RF negative. Systemic arthritis was rarely reported in this brief time period.

TABLE 18

Number of cases and percentages of JIA subtypes

JIA subtype	Number of cases	%
Oligoarthritis	14	34.1
Enthesitis related	6	14.6
Polyarthritis RF–	5	12.2
Psoriatic	4	9.7
Polyarthritis RF+	2	4.8
Systemic	1	2.4
Unclassified	2	4.8

Conclusion

During the first three months of active surveillance, an average of 39 new JIA cases were reported per month, with the majority of patients being reported from paediatric rheumatology subspecialty centres. These data suggest that approximately 470 newly diagnosed cases of JIA are seen in Canada annually. Patients were reported from all provinces, with a distribution consistent with child population. In this early data collection, children with First Nations ethnicity appear over-represented amongst children with JIA. These data are consistent with reports of a high incidence of arthritis among adult Canadian First Nations people, but there have been few accurate reports of the incidence of juvenile arthritis in this group.

The clinical presentation of the patients reported to date in this study is consistent with previously reported studies, with joint pain, swelling and stiffness being commonly reported. It is important to note that joint pain does not occur in 10% of patients and that joint swelling was not seen in 15%; often the lack of joint pain is a factor leading to delayed diagnosis. The most common JIA subtype is oligoarthritis. Interestingly, two JIA subtypes that are frequently not included in studies, enthesitis related arthritis and psoriatic arthritis, are quite commonly seen in this study. Systemic arthritis was rare, with only one case reported during the first three-month study period.

The data from this study’s early phase are already showing important information about the number of children with JIA in Canada. Demonstrating the distribution of cases across the country will

be extremely valuable in advocating for appropriate medical resources for these children. In addition, early data on subtypes of JIA are already showing some interesting trends, substantiating the need to study children with enthesitis related arthritis and psoriatic arthritis.

Principal investigator

- Lori B. Tucker, MD, Division of Pediatric Rheumatology, British Columbia's Children's Hospital, 4500 Oak St, Vancouver BC V6H 3V1; tel. 604-875-2437; fax: 604-875-3141; e-mail: ltucker@cw.bc.ca

- Paul Dancey, MD, Janeway Children's Health and Rehabilitation Centre, Faculty of Medicine at Memorial University
- Adam Huber, MD, MSc, Division of Pediatric Rheumatology, IWK Health Centre, Dalhousie University

Co-investigators

- Brian Feldman, MD, University of Toronto
- Claudia Lagacé, Public Health Agency of Canada
- Kiem Oen, MD, University of Manitoba
- Rayfel Schneider, MD, BCh, University of Toronto



Kernicterus

January 2007 to December 2008

Highlights

- Kernicterus (chronic bilirubin encephalopathy) continues to occur in Canada with 10 confirmed cases.
- ABO incompatibility and G6PD deficiency are the most common identified causes of acute bilirubin encephalopathy leading to kernicterus.
- Nine confirmed cases had abnormal auditory brainstem responses and eight had confirmatory MRI scans of the brain.

Background

Hyperbilirubinemia remains the most common cause of neonatal hospital readmissions in Canada and the United States, with the risk of acute bilirubin encephalopathy and in severe cases, kernicterus.

The clinical features of kernicterus (chronic bilirubin encephalopathy) include athetoid cerebral palsy, dystonia (hypertonia or hypotonia), sensorineural hearing loss, dental enamel dysplasia, oculomotor impairments (including paralysis of the upward gaze) and intellectual and developmental delays. On MRI, children with kernicterus can show increased signal intensity in the basal ganglia (especially the posteromedial border of the globus pallidus) and the subthalamic nuclei.

Historically, kernicterus was secondary to hyperbilirubinemia from hemolysis, usually due to Rh isoimmunization and ABO incompatibility. From the 1950s to the 1980s, several developments resulted in a marked reduction of kernicterus, such as the introduction of exchange transfusions, the availability of RhoGAM for Rh negative mothers, routine testing of antibody titers during pregnancy, cord blood testing for blood group and antiglobulin antibodies (Coombs' testing) in neonates, and phototherapy in treating hyperbilirubinemia.

Over the last decade, the incidence of kernicterus appears to have increased again. A recent surveillance study on severe hyperbilirubinemia demonstrated that ABO incompatibility, followed by G6PD deficiency, were the most common causes for severe hyperbilirubinemia in Canada,

and that almost three-quarters of newborns were readmitted to hospital at a mean age of less than five days of life. With early detection of severe neonatal hyperbilirubinemia, both acute bilirubin encephalopathy and kernicterus could be prevented.

Objectives

- 1) To establish the incidence of kernicterus and/or bilirubin-induced neurologic dysfunction (BIND) in Canada.
- 2) To identify epidemiological and medical risk factors possibly useful in preventing this disease, whether it is through selective screening of newborns for serum bilirubin, G6PD and Coombs' testing or by measuring serum bilirubin in all newborns prior to discharge from hospital.

Case definition

Report any child up to six years of age with:

- a history of significant neonatal hyperbilirubinemia (peak bilirubin $>425\mu\text{mol/L}$ or exchange transfusion) **and**
- two or more of the following symptoms:
 - a) extrapyramidal disorders (e.g., dystonia, athetosis)
 - b) other movement disorder (spasticity or hypotonia)
 - c) gaze abnormalities
 - d) sensorineural hearing loss
 - e) intellectual deficits
 - f) enamel dysplasia of the deciduous teeth

OR

- abnormal MRI with bilateral lesions of basal ganglia/midbrain (globus pallidus +

subthalamic nucleus) with a history of neonatal hyperbilirubinemia.

Exclusion criteria

- Born at less than 35 weeks gestational age.
- Metabolic condition with basal ganglia involvement (e.g., glutaric acidemia type II, pyruvate dehydrogenase deficiency, Hallervorden-Spatz disease, neurofibromatosis type I, or children with carbon monoxide poisoning).

Results

TABLE 19

Kernicterus cases in 2007

Reported	Duplicates	Excluded	Pending	Confirmed
16	3	1	2	10

In the first year of surveillance, 16 cases of kernicterus (chronic bilirubin encephalopathy) were reported. Of these reports, 10 have been confirmed and two are incomplete, as detailed questionnaires are pending. Nine of the confirmed cases are under one year of age. The range of peak bilirubin was 432–795 $\mu\text{mol/L}$ (mean 549 $\mu\text{mol/L}$). The etiologies included ABO incompatibility ($n=3$), G6PD deficiency ($n=2$), one each of anti-c antibodies and *E. coli* sepsis, and three cases where etiology was not reported. All cases had neurological findings such as dystonia, hypotonia, oral motor problem/swallowing difficulties, seizures, opisthotonus or psychomotor developmental delay. Abnormal auditory brainstem responses were present in all but one case, and confirmatory MRI scans of the brain showing bilateral lesions of basal ganglia/mid-brain were present in all but two cases.

Discussion

In the first year of surveillance, 10 cases of children with kernicterus were confirmed. In all but one case, the diagnosis was established at less than one year of age. Data collection was complete regarding peak serum bilirubin, neurological findings and neuro-imaging. Taking this very conservative estimate of 10 new cases of kernicterus in children born in 2007, this would give an incidence of 1 in

30,000 births (assuming a birth rate of 300,000 per year). This interpretation regarding the incidence of kernicterus (chronic bilirubin encephalopathy) is preliminary, as detailed questionnaires on cases reported in the later part of 2007 have not yet been completed. Depending on the outcome analysis of these cases, the incidence might need to be recalculated.

Data received in the first year allowed the establishment of the study objectives; specifically, the estimation of the kernicterus incidence and the identification of an etiology in the majority of cases. A preliminary study incidence estimate would be very conservative, given that this is voluntary reporting and that the establishment of kernicterus as a diagnosis is often difficult and may be delayed.

ABO incompatibility and G6PD deficiency were the most common etiologies. This is in keeping with the previous CPSP study on severe neonatal hyperbilirubinemia in Canada. Information regarding the infant's blood group, Coomb's test and G6PD status are unknown at the time when most newborns are discharged home. This highlights the importance of careful monitoring for hyperbilirubinemia in newborns at the time of discharge and in follow-up. Newborns that develop severe hyperbilirubinemia and subsequently kernicterus may have risk factors that are unknown until the severe hyperbilirubinemia develops. Therefore, careful surveillance and follow-up, as expressed in the recently updated CPS guidelines, are needed to attempt to prevent kernicterus. The document is entitled *Guidelines for Detection, Management and Prevention of Hyperbilirubinemia in Term and Late Preterm Newborn Infants (35 or more weeks' gestation)* and was published in June 2007.

Conclusion

Kernicterus continues to occur in Canada. Analysis of preliminary data suggests that the incidence of kernicterus may be higher than previous estimates in the literature. The most common etiologies for kernicterus appear to be ABO incompatibility and G6PD deficiency.

Given that there have been changes to the CPS guidelines on the management of neonatal hyperbilirubinemia, continued surveillance is necessary to assess the effectiveness of these guidelines and if additional strategies need to be implemented to prevent kernicterus.

Principal investigator

- Michael Sgro, MD, FRCPC, University of Toronto, Department of Paediatrics, St. Michael's Hospital, Room 014, 15th floor,

Cardinal Carter Wing, 30 Bond St, Toronto ON M5B 1W8; tel: 416-864-6060, ext. 8273; fax: 416-864-6073; e-mail: sgrom@smh.toronto.on.ca

Co-investigators

- Douglas M. Campbell, MD, FRCPC, University of Toronto
- Shafagh Fallah, PhD, University of Toronto
- Vibhuti Shah, MD, FRCPC, University of Toronto

Medium-chain acyl-coenzyme A dehydrogenase deficiency

September 2005 to August 2008

Highlights

- Ten cases of MCAD deficiency were confirmed in 2007.
- Two cases of MCAD were detected in deceased patients from provinces that do not have newborn screening programs.
- There were no deaths in provinces that have newborn screening programs.

Background

Medium-chain acyl-coenzyme A dehydrogenase (MCAD) deficiency is the most common autosomal recessive inherited fatty acid oxidation disorder, with an incidence of about one in 10,000–20,000. MCAD is one of the enzymes involved in the fatty acid beta-oxidation pathway. The most common presentation is during infancy, when a relatively well child may deteriorate during an acute illness and develop hypoglycemia, vomiting, mild hepatomegaly and altered sensorium. Some of the other biochemical features include hypoketosis, mild hyperammonemia and mild elevation in liver enzymes. If unrecognized, there is deterioration with coma, seizures, residual neurological deficits and subsequent developmental delay. The mortality risk can be up to 25% at the time of the initial presentation. Another clinical presentation is unexplained sudden infant death syndrome (SIDS). Interestingly, some patients with this disorder can also remain asymptomatic, thus leading to great variability in the clinical phenotype.

The definitive diagnosis is made by the interpretation of plasma acylcarnitine (elevation of C6–C10 and predominant octanoylcarnitine) and/or elevated suberyl and hexanoylglycine in urine and dicarboxylic aciduria. DNA analysis can confirm the diagnosis by the presence of the 985 A>G mutation (common in the northern European population) or by one of the rare mutations. If needed, measuring the MCAD activity in skin fibroblasts can also help in the diagnosis.

Treatment of this condition involves avoiding fasting and ensuring adequate glucose intake during acute illnesses (in accordance with management protocol). For children, a carnitine dose of 100 mg/kg three times per day is given; however, there is still some controversy as to the benefits of its prolonged use. With the advent of newborn screening and the use of tandem mass spectrometry, this disorder is now being screened in the neonatal period in a number of countries including Canada, where seven provinces and one territory (BC, SK, ON, NB, NS, PE, NL and YK) have screening programs. MCAD deficiency has an excellent prognosis when treated early and has significant genetic implications for future pregnancies and other family members. The exact incidence of MCAD deficiency in Canada is still largely unknown due to the lack of universal newborn screening programs.

Objectives

Primary objectives

- 1) Estimate the incidence of MCAD deficiency in Canada.
- 2) Describe the health status of children with MCAD deficiency in Canada at the time of diagnosis.

Secondary objectives

- 1) Determine if more children are diagnosed with MCAD deficiency in provinces with screening programs than in those without such programs.
- 2) Determine if the health status of children diagnosed by screening programs at the time of diagnosis differs from children diagnosed due to symptoms or family history.

Case definition

Report any patients newly diagnosed with MCAD deficiency following investigations initiated due to any of the following: newborn screening, clinical symptoms, and diagnosis in an affected family member or post-mortem diagnosis. A child will be considered to have a diagnosis of MCAD deficiency if at least **ONE** of the following biochemical/genetic diagnostic criteria is met:

- 1) Elevated plasma C6 to C10 acylcarnitines with predominance of C8 (octanoylcarnitine);
- 2) Elevated urinary organic acids: phenylpropionylglycine, suberylglycine, hexanoylglycine, and medium chain dicarboxylic acids (C6>C8>C10);
- 3) Molecular genetic studies confirming the presence of the 985 A>G mutation, or other less common mutations;
- 4) Skin fibroblasts acylcarnitine probe assay demonstrating accumulation of characteristic acylcarnitines; or
- 5) Skin fibroblasts enzyme studies showing reduced activity of MCAD.

In the presence of the following clinical features or biochemical findings:

- Vomiting, hepatomegaly and altered sensorium
- Hypoglycemia and elevated liver enzymes.

Results/discussion

TABLE 20

Medium-chain acyl-coenzyme A dehydrogenase deficiency cases in 2007

Reported	Duplicates	Excluded	Pending	Confirmed
24	9	2	3	10

In 2007, 24 cases of MCAD deficiency were reported. Of these 24 cases, 10 were confirmed and three are pending confirmation. Of the 10 confirmed cases, six were detected in provinces with a newborn screening program for MCAD deficiency. For the first year since the study began in 2005, four cases were reported from provinces without a screening program. Three of these four

children are deceased, and the child who is not deceased was picked up after the child became symptomatic. In 2006, there were 17 potential cases with 14 confirmed. All cases were discovered through newborn screening and a positive family screening, except for one patient who was symptomatic at two years. In 2005, there were three potential and two confirmed cases. Both confirmed cases were from western Canada and were detected through newborn screening.

Conclusion

The MCAD deficiency study through the CPSP is a very good means of identifying cases and of acquiring data on a timely basis for all patients with MCAD deficiency. To improve the identification of cases, this study includes representation from Canadian pathologists, particularly coroners, whose participation is important since, unfortunately, 25% of patients with MCAD deficiency die at their first presentation. Metabolic laboratory directors are also participating in this study. Ongoing education of paediatricians and family doctors is essential, as MCAD deficiency has a highly variable clinical phenotype. Family screening should also be performed when an infant is detected with MCAD deficiency through newborn screening, as a number of cases have been detected when family screening was initiated. So far, all cases detected on newborn screening have been asymptomatic. Two confirmed deceased MCAD cases were reported from provinces that are not doing newborn screening for MCAD. Consequently, the results of this study reinforce the importance of initiating newborn screening for MCAD in all Canadian provinces and territories, as MCAD has an excellent prognosis once the diagnosis is made.

Principal investigator

- Chitra Prasad, MD, FRCPC, FCCMG, Metabolism Program, University of Western Ontario, Children's Hospital of Western Ontario, 800 Commissioners Rd E, London ON N6C 2V5; tel.: 519-685-8140; fax: 519-685-8214; e-mail: Chitra.Prasad@lhsc.on.ca

Co-investigators

- Pranesh Chakraborty, MD, FRCPC, FCCMG, University of Ottawa
- Sarah Dyack, MD, Dalhousie University
- Jonathan B. Kronick, PhD, MD, Dalhousie University
- C.A. Rupa, PhD, FCCMG, University of Western Ontario

- Kathy Nixon Speechley, PhD, University of Western Ontario

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Non-type 1 diabetes mellitus

April 2006 to March 2008

Highlights

- Nearly 65% of all NT1DM cases are type 2 diabetes mellitus (T2DM).
- Obesity/overweight appears to be the single most important risk factor for T2DM.
- At diagnosis, nearly 60% of children with T2DM had at least one obesity-related co-morbid condition.
- Children developing medication-induced diabetes mellitus seem to have different risk factors than children who develop T2DM.
- Study results identify the need for national randomized control trials of efficacy and safety of various treatment modalities for T2DM in the paediatric population.

Background

Diabetes mellitus (DM) in children has evolved in the past decade, from the most common diagnosis of type 1 diabetes mellitus (T1DM) to a more complex differential diagnosis comprising type 2 diabetes mellitus (T2DM), monogenic forms of diabetes and secondary diabetes, including medication-induced diabetes mellitus (MID) (e.g., steroids, L-asparaginase, tacrolimus). The increasing prevalence of T2DM is associated with the rapidly increasing prevalence of childhood obesity. Additionally, more cases of monogenic diabetes and MID may be mediated directly or indirectly by increased body weight, and both can be difficult to distinguish from T2DM.

Data on the incidence and prevalence of non-type 1 diabetes mellitus (NT1DM) in Canadian children are limited. There is currently a global effort to conduct population incidence and prevalence studies to quantify the extent of the problem. It is imperative that Canadian data be obtained because of Canada's unique ethnic, cultural, geographic and behavioural characteristics, and in order to gain a better understanding of the magnitude, characteristics and public health consequences of this disease. In addition to the participation of all paediatricians enrolled in the CPSP (n=2,400), this study will include a sample of family physicians (n=100) and adult endocrinologists (n=48) who were recruited from the College of Family Physicians National Research System and endocrine registries, respectively, in order to maximize case ascertainment.

Objectives

- 1) Determine the incidence of NT1DM among Canadian children.
- 2) Determine the incidence of T2DM among Canadian children.
- 3) Describe the clinical features of T2DM at diagnosis that aid in the differentiation of T2DM from T1DM.
- 4) Identify co-existing morbidity associated with T2DM at diagnosis.

Case definition

Report any patient less than 18 years of age with a diagnosis of diabetes and clinical features not consistent with classic type 1 diabetes (non-obese child with symptomatic acute hyperglycemia).

Clinical features suggestive of NT1DM include:

- Obesity (body mass index > 95th percentile for age and gender)
- Family history of T2DM in a first or second degree relative(s)
- Belonging to an ethnic group at high risk for non-type 1 diabetes (e.g., Aboriginal, African, Hispanic, South-Asian)
- A history of exposure to diabetes in utero (diagnosed before or during pregnancy)
- Acanthosis nigricans
- Polycystic ovarian syndrome
- Diabetes in a person with a syndrome often associated with type 2 diabetes (Prader-Willi Syndrome)

- Diabetes in a non-obese patient with at least one first degree relative and/or two second degree relatives with diabetes
- Minimal or no insulin requirement with a normal or near normal hemoglobin A1c level (4–6%) one year after diagnosis
- A diagnosis of diabetes while on medical therapy with a known diabetogenic medication (e.g., glucocorticoid, L-asparaginase, cyclosporine, tacrolimus, atypical antipsychotic, anticonvulsant)

Exclusion criteria

- Do not report any cystic fibrosis-related diabetes or patients in critical care settings requiring short-term insulin therapy for stress hyperglycemia.

Results

TABLE 21

Non-type 1 diabetes cases in 2007

Reported	Duplicates	Excluded	Pending	Confirmed
217	6	25	12	174

From April 1, 2006 to December 31, 2007 a total of 389 cases of NT1DM were reported (Table 22). Of the confirmed cases, 224 were reported by paediatric endocrinologists, 43 by paediatricians, 14 by family physicians and three by adult endocrinologists. Forty-one cases were eliminated due to diagnosis of NT1DM outside the reporting period or failure to meet the criteria for diabetes as defined by the Canadian Diabetes Association.

TABLE 22

Non-type 1 diabetes cases April 1, 2006 to December 31, 2007

Reported	Duplicates	Excluded	Pending	Confirmed
389	15	41	49	284

TABLE 23

Classification of confirmed cases of non-type 1 diabetes mellitus

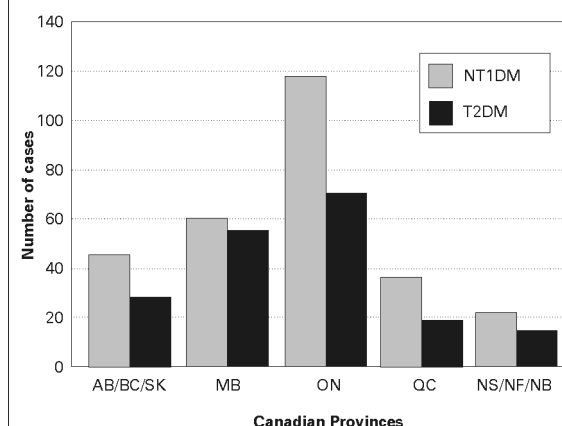
Confirmed	T2DM*	MID†	Monogenic DM	Indeterminate
284	184	49	22	29

* Type 2 diabetes mellitus

† Medication-induced diabetes

FIGURE 6

Provincial distribution of NT1DM and T2DM cases



Reporting of NT1DM varied from province to province. Figure 6 shows the provincial variation in the reporting of NT1DM and T2DM. Ontario and Manitoba had the highest rates of reporting.

TABLE 24

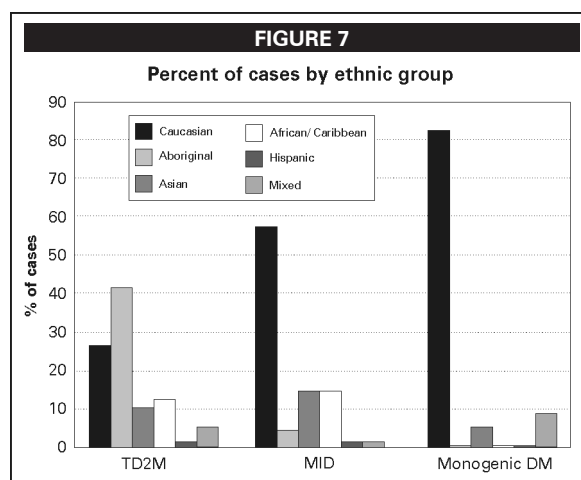
Epidemiological and demographic data

	T2DM (n=184)	MID (n=49)	Monogenic DM (n=22)
Mean age (years) (95% CI)	13.8 (13.4, 14.1)	13.5 (12.5, 14.4)	8.0 (5.2, 10.8)
Female: male ratio	1.5:1	1.4:1	1.2:1
Ethnicity (%) (95% CI)			
Caucasian	27 (21, 34)	57 (42, 71)	82 (60, 95)
Aboriginal	41 (34, 49)	4 (0.5, 14)	0
Asian	10 (6, 16)	14 (6, 27)	5 (0.1, 23)
African/Caribbean	12 (8, 18)	14 (6, 27)	0
Hispanic	2 (0.5, 5)	2 (0.05, 11)	0
Mixed	5 (2, 9)	2 (0.05, 11)	9 (1, 29)
Mean BMI (95% CI)	32.4 (31.3, 33.4)	23.3 (21.4, 25.2)	17.4 (15.3, 19.4)
Obesity (%)	88 (163/186)	27 (13/49)	5 (1/22)
Positive family history* (%)	83 (152/184)	49 (24/49)	86 (19/22)
> 1 co-morbid condition at diagnosis (%)	59 (108/184)	31 (15/49)	18 (4/22)
Treatment (%)			
Insulin	3 (5/184)	27 (13/49)	14 (3/22)
Oral hypoglycemics	1 (2/184)	0	5 (1/22)
Lifestyle counselling	33 (61/184)	22 (11/49)	64 (14/22)
Insulin and LC†	24 (45/184)	31 (15/49)	5 (1/22)
OH‡ and LC	23 (42/184)	0	5 (1/22)
Insulin, OH, and LC	15 (27/184)	0	0
No treatment	0	12 (6/49)	1 (1/22)

* First or second degree relative with diabetes

† Lifestyle counselling

‡ Oral hypoglycemics



Discussion

Based on a review of diabetes clinics at the Children's Hospital, Winnipeg, Manitoba and The Hospital for Sick Children, Toronto, Ontario, it was estimated that 200 cases of T2DM, 50 cases of MID and 100 cases of monogenic diabetes would be identified annually. Preliminary data obtained from this study reveal lower numbers of cases in all three categories of NT1DM. This may indicate under-reporting by participating physicians or a pre-study overestimation of the incidence of T2DM, MID and monogenic diabetes in Canadian children.

Children with T2DM presented at a mean age of 13.8 years. Obesity/overweight appears to be the single most important risk factor for T2DM, affecting nearly 90% of reported cases of clinically diagnosed T2DM. The mean HbA1c at presentation of T2DM was 9.6% (95% CI: 9.1%, 10.1%). Of these cases, 41% (35/86) presented with ketosis and 9% (17/184) with ketoacidosis. The presence of ketosis may indicate a diagnosis of T1DM in an obese child. Close attention to the clinical course and measurement of pancreatic antibody levels may help clarify the diagnosis, necessitating more readily available laboratory testing for pancreatic antibodies. Most children with T2DM have a positive family history of diabetes and many belong to high-risk ethnic groups; however, 27% of children with T2DM in this study were Caucasian. These findings stress the importance of screening **all** obese adolescent

and pre-adolescent children for diabetes as well as for other features of the metabolic syndrome. Fifty-nine percent (59%) of children diagnosed with T2DM had at least one obesity-related co-morbid condition **at diagnosis**. These preliminary data underscore the critical need for primary prevention programs targeted towards childhood obesity, which are essential in the prevention of T2DM and other obesity related co-morbidities.

The treatment of T2DM varies considerably depending on physician experience, physician bias and local medical culture. In this study, 33% of patients with T2DM were treated with lifestyle counselling alone. Lifestyle counselling in combination with an oral hypoglycemic, insulin, and both an oral hypoglycemic and insulin were used in treating 23%, 24% and 15% of patients, respectively. This reflects the lack of a standardized approach to the treatment of childhood T2DM as well as the lack of heterogeneity in presentation (e.g., asymptomatic to ketoacidosis). Study results will provide background data required to motivate the initiation of a national randomized control trial examining the efficacy and safety of various treatment modalities for T2DM in children and adolescents.

As rates of childhood obesity and T2DM increase, MID may also occur more frequently, mediated directly or indirectly by increased body weight. The study hypothesis was that children who develop MID have similar risk factors to children who develop T2DM. Preliminary data analysis shows that this may not be the case. Children with MID are more likely to be Caucasian, have lower BMI, have less acanthosis nigricans and have lower rates of T2DM in family members than those with T2DM. Accordingly, identification of children at risk for the development of MID is not possible using traditional risk factors for T2DM. Of note, these are preliminary data; long-term, prospective studies are needed to identify youth with MID who are at future risk of developing T2DM.

Conclusion

National surveillance for NT1DM in Canadian children concludes March 31, 2008, completing

two years of surveillance. This study is vital in providing epidemiological and demographic data on Canadian children affected with NT1DM and specifically, obesity-related T2DM. These data will provide a foundation upon which specific paediatric health promotion and disease prevention programs can be established.

Moreover, this study establishes a collaborative approach that will enable repeated estimates of NT1DM in the future. Therefore, this project not only provides incidence rates of T2DM and other forms of NT1DM, but also allows for future comparison of epidemiological data, recognition of national trends, and the assessment of the efficacy of health promotion and disease prevention programs. Furthermore, the Canadian incidence rate of NT1DM, and specifically obesity-related T2DM, will be compared to other countries through collaboration with international surveillance units (e.g., the British Paediatric Surveillance Unit). Support from reporting physicians for the duration of this study is greatly appreciated by all investigators and collaborators.

Principal investigators

- Shazhan Amed, MD, Division of Endocrinology, The Hospital for Sick Children, 555 University Ave, Toronto ON M5G 1X8; tel.: 416-813-7654 ext 2947; fax: 416-813-6304; e-mail: shazhan.amed@sickkids.ca
- Heather Dean, MD, Division of Endocrinology and Metabolism, Children's Hospital of Winnipeg, University of Manitoba
- Jill Hamilton, MD, Division of Endocrinology, The Hospital for Sick Children

Co-investigators

- Gillian Booth, MD, University of Toronto
- David Dannenbaum, MD, McGill University
- Stasia Hadjiyannakis, MD, Children's Hospital of Eastern Ontario
- Tessa Laubscher, MB ChB, University of Saskatchewan
- Constadina Panagiotopoulos, MD, BC Children's Hospital
- Elizabeth Sellers, MD, Children's Hospital of Winnipeg

Severe combined immunodeficiency

April 2004 to March 2009

Highlights

- Six cases of SCID were confirmed in 2007.
- The average age at the SCID diagnosis is steadily decreasing; it was three months in 2007. Earlier diagnosis carries a better prognosis.
- All the cases were referred for bone marrow transplant.

Background

Severe combined immunodeficiency (SCID) is a group of rare genetic disorders characterized by profound abnormalities in T and B cells and natural killer cell development and function. SCID is a serious, life-threatening condition with high morbidity and mortality.

As part of the strategy to reduce the incidence and severity of tuberculosis (TB) in children living on reserves with a high incidence of TB, the First Nations and Inuit Health Branch (FNIHB) of Health Canada has recommended the use of the live, attenuated BCG (bacille Calmette-Guérin) vaccine for newborns. However, concerns regarding both the efficacy and the safety of this vaccine have prompted the FNIHB to reconsider this recommendation. Six cases of disseminated BCG infection in First Nations and Inuit children were reported between 1993 and 2002. All six children died: four had SCID, one was HIV positive and one had another immunodeficiency. The observed rate of disseminated BCG infection in First Nations and Inuit populations in Canada is 205 cases (CI 42–600) per 1,000,000 doses, which greatly exceeds global estimates of 0.19–1.56 cases per 1,000,000 doses given.

While no Canadian data are available on the incidence of SCID, it may be that this unusual rate of disseminated BCG infection is associated with a high incidence rate of SCID in the Aboriginal population. Hence, data on the incidence of SCID are required to make evidence-based decisions about the risks and benefits of continuing to offer BCG vaccine to First Nations and Inuit children on reserves with high TB incidence, and to guide future decisions regarding the reduction or discontinuation of the BCG vaccination.

SCID was first reported more than 50 years ago. In the past two decades, great advances have been made in understanding and treating the disorder. A variety of molecular defects have recently been found to cause SCID, including defects in the gene encoding the common gamma chain (X-linked form), adenosine deaminase (ADA) deficiency, interleukin-7 receptor deficiency, Janus tyrosine kinase-3 (JAK3) deficiency and recombina- activating gene (RAG-1 and RAG-2) deficiency. The two most common forms of SCID are the X-linked SCID (about 50% of all cases) and those that are due to an ADA deficiency (about 15–20%).

A general estimate of the incidence of SCID is 1 in 75,000–100,000 live births. Higher-than-expected rates are seen in Switzerland, at 24.3 in 100,000 live births, and in the United States' Navajo population, at 52 in 100,000 live births. Until this study, no Canadian incidence data for SCID were available.

Objectives

- 1) To estimate the incidence of SCID in Canada.
- 2) To estimate the incidence of SCID in Aboriginal children in Canada.
- 3) To describe the basic demographics, clinical features and outcomes of SCID in Canada.

Case definition

Report any child less than two years of age with the clinical features of SCID (i.e., chronic diarrhea, recurrent pneumonia, failure to thrive, persistent thrush, opportunistic infections, etc.) **and** at least one of the following:

- Absolute lymphocyte count of less than 3,000/mm³ or less than 20% CD3⁺ T cells;
- Familial history of primary immunodeficiency.

Exclusion criteria

Exclude infants with HIV infection or cystic fibrosis.

Results/discussion

There were six confirmed cases of SCID in 2007. Another eight cases are pending, awaiting detailed case reports and/or further immunological data.

TABLE 25

Severe combined immunodeficiency cases in 2007

Reported	Duplicates	Excluded	Pending	Confirmed
20	6	0	8	6

Of the confirmed cases, four are male and two are female. All were born in Canada; one is an Aboriginal child. The average age at diagnosis is three months (range 0–8 months). Three of the confirmed cases were of the ADA deficiency SCID-type: one was due to Zap 70 mutation, one was autosomal recessive, and another was X-linked.

The main clinical features included interstitial pneumonia and failure to thrive. Five of the confirmed cases were referred for bone marrow transplant. At the time of reporting, three had received the transplant, one was scheduled to receive it in March, and one died before the transplant. Two of the cases were in the hospital; two were discharged when the reports were received.

There were more cases reported in 2007 ($n=20$) than in 2006 ($n=11$) and 2005 ($n=10$). Six cases were confirmed this year compared to three last year, with 2005 having the highest number of confirmed cases ($n=7$). One case involving an Aboriginal child was confirmed in both 2006 and 2007. The appearance of Aboriginal cases in the last two years will help in estimating the SCID incidence in this ethnic group of children, which is a secondary objective of the study. The confirmed cases in 2007 were diagnosed at a younger age

than those reported in 2006 and 2005 (3 months versus 5.8 months and 10 months). This tendency is welcomed, as the earlier the SCID diagnosis is established, the better the prognosis, and a bone marrow transplant can be performed before the appearance of overwhelming infections.

Conclusion

Based on existing estimates for the rate of SCID and the annual birth rate in Canada, the expected number of new cases of SCID is three to 17 per year. With an average of five confirmed cases annually, the study is within the range of expected numbers of new cases. Annual rates of SCID will be determined when all of the reported cases for a one-year period are diagnosed and analyzed. This study has been extended until March 2009 and may continue beyond then if warranted.

Principal investigator

- Ezzat Farzad, MD, Office of Community Medicine, First Nations and Inuit Health Branch, Health Canada, Jeanne Mance Building, 7th Floor, Tunney's Pasture, AL 1907D, Ottawa ON K1A 0K9; tel.: 613-941-6133; fax: 613-954-9715; e-mail: ezzat_farzad@hc-sc.gc.ca

Co-investigators

- Martin A. Champagne, MD, University of Montreal
- Joanne Embree, MD, University of Manitoba
- Marene Gatali, MHSc, Health Canada
- Anne Junker, MD, University of British Columbia
- Joanne Langley, MD, Dalhousie University
- Richard Long, MD, University of Alberta
- Louise Pelletier, MD, Public Health Agency of Canada
- Kirk R. Schultz, MD, University of British Columbia
- Wadieh Yacoub, MB BCH, Health Canada

Transfusion-related acute lung injury

September 2005 to August 2008

Highlights

- TRALI is currently the most common cause of transfusion-related death in adults.
- The incidence of TRALI in the paediatric population is unknown.

Background

Transfusion of blood products can lead to various transfusion reactions. Transfusion-related acute lung injury (TRALI), although rare, is the leading cause of transfusion-related fatalities reported to the United States Food and Drug Administration. Patients develop acute lung injury rapidly – within six hours of initiating a transfusion of any blood product containing plasma (red blood cells, platelets, or fresh frozen plasma). Extremely small volumes of plasma can trigger the reaction. Symptoms consist of respiratory distress, hypoxemia ($\text{PaO}_2/\text{FiO}_2 \leq 300$ or $\text{SpO}_2 < 90\%$ on room air), fever, tachycardia and hypotension. New bilateral pulmonary infiltrates, usually alveolar and interstitial, appear on the chest radiograph. Cardiac dysfunction and/or circulatory overload have to be excluded. All patients require supplemental oxygen; 70% will need mechanical ventilation. TRALI patients usually have a good prognosis and improve rapidly (<96 hours) without long-term sequelae. However, the mortality rate is approximately 6%.

The incidence of TRALI in the paediatric population is unknown. Even though TRALI is becoming recognized more frequently in clinical practice and is receiving greater attention and description in the literature, it likely remains under-diagnosed and under-reported. This study is the first to assess the incidence, presentation and burden of TRALI in the paediatric population. Collecting national epidemiological data in the paediatric population will help to better describe the clinical presentation of TRALI, raise awareness and inform prevention strategies.

Objectives

- 1) Determine the incidence of TRALI in the paediatric population using a standardized definition.

- 2) Describe the characteristics of patients and the clinical signs and symptoms associated with TRALI in the paediatric population.
- 3) Describe the treatment and outcome of TRALI in paediatric patients.
- 4) Compare paediatric incidence and demographic data with the adult population data published in the literature.
- 5) Promote education and awareness of this rare disease among paediatric health care professionals.

Case definition

TRALI is a clinical and radiological diagnosis and is not dependent on the results of laboratory tests or any proposed pathophysiologic mechanism. Children up to and including 18 years of age with TRALI or possible TRALI are reported.

TRALI inclusion criteria (all three criteria must be present)

- New onset of acute lung injury (ALI) during or within six hours of transfusion
- Hypoxemia: $\text{PaO}_2/\text{FiO}_2 \leq 300$ or $\text{SpO}_2 < 90\%$ on room air
- Bilateral infiltrates on frontal chest radiograph

TRALI exclusion criteria

- Evidence of left atrial hypertension (i.e., circulatory overload)
- Pre-existing acute lung injury before transfusion
- Temporal relationship to an alternative risk factor for ALI

Possible TRALI

Same TRALI inclusion and exclusion criteria, except that a clear temporal relationship to an alternative risk for ALI is present, such as the following:

Direct lung injury

Aspiration
Pneumonia
Toxic inhalation
Lung contusion
Near drowning

Indirect lung injury

Severe sepsis
Shock
Multiple trauma
Burn injury
Acute pancreatitis
Cardiopulmonary bypass
Drug overdose

The case definition is a consensus definition from an International Consensus Conference on TRALI held in 2004.

Results

TABLE 26

Transfusion-related acute lung injury cases in 2007

Reported	Duplicates	Excluded	Pending	Confirmed
1	0	0	0	1

One case of TRALI was confirmed in 2007. A 35-week premature newborn with severe intra-uterine growth retardation and VACTER malformations underwent, at one month of age, major cardiac surgery for tetralogy of Fallot. The patient received multiple transfusions during the two-hour surgical procedure: 33 cc/kg of plasma over five minutes, followed by 18 cc/kg of apheresis platelets over two hours, and then an allogenic red blood cell unit (volume not available) over 30 minutes. TRALI occurred a few minutes later, shortly after the end of the extracorporeal circulation.

The patient was already intubated and mechanically ventilated for the surgery. He had desaturation episodes requiring increased oxygen administration (100%) as well as increased ventilatory pressures (inspiratory pressure increased from 24 to 40 cm H₂O). The PaO₂/FiO₂ ratio was 52. According to the medical team, the patient did not present cardiac dysfunction. Central venous pressure and wedge pressures varied from 13 to 16, with a maximum of 21 on one occasion. In the following hours, the patient required high frequency ventilation, nitric oxide administration (20 ppm), sedation with paralyzing agents, fluid bolus ≥ 10 cc/kg and inotropes. He also developed a pneumothorax. After the episode of TRALI, he was ventilated for a total of 10 days, stayed

in the paediatric intensive care unit for 13 days and was discharged home seven days later. The TRALI episode was reported to the blood bank. The medical team considered that this TRALI did put the patient in danger of dying but did not cause long-term morbidity.

Conclusion

Three cases of TRALI have been declared since the beginning of the study. The one described in this report is the second case of an infant presenting TRALI shortly after extracorporeal circulation for surgery of congenital heart disease. Although the medical team believes this case is TRALI, the fact that there was another risk factor of ALI involved (extracorporeal circulation) means this case has to be considered as a *possible* TRALI. It will be interesting to see if similar cases are reported in subsequent years. If so, the medical team (cardiac surgeons, anaesthetists and paediatric intensive care specialists) would need to be informed of this potential risk factor.

TRALI is a very rare phenomenon. Nevertheless, it is expected that more cases would have been declared so far. A compounding factor is that TRALI presents as a clinical syndrome without a pathognomic confirmatory laboratory test; therefore, under-diagnosis and under-reporting are highly suspected. Other possible hypotheses for the rarity of cases include the following:

- 1) The TRALI definition is not suitable in paediatrics, as it could be more difficult to evaluate ALI in small children.
- 2) The exclusion criteria discounting patients with previous ALI is restrictive and might exclude many neonates and paediatric intensive care unit patients that are more at risk.
- 3) The pathophysiology is different in children and their transfusion-related respiratory distress is mostly due to an aetiology other than TRALI (i.e., cytokines).

The continuation of the TRALI surveillance could help clarify all these possibilities in the paediatric population. If more cases are declared, and if more data are captured, a comparative analysis could be performed using the capture-recapture

method, with TRALI cases reported through the Transfusion Transmitted Injuries Surveillance System.

This study remains a useful tool to promote education and awareness among health care professionals of this uncommon transfusion reaction. Information on TRALI will help paediatricians to better recognize this serious life-threatening complication and to acknowledge the need to immediately alert the blood bank to prevent further distribution of the same donor blood to other patients, thereby avoiding further TRALI episodes.

Principal investigator

- France Gauvin, MD, Université de Montréal, Sainte-Justine UHC, 3175 ch

Côte-Sainte-Catherine, Montréal QC
H3T 1C5; tel.: 514-345-4931, ext. 6812;
fax: 514-345-4822; e-mail: france_gauvin@
ssss.gouv.qc.ca (representing a network of
nine investigators from across Canada)

Co-investigators

- Gilles Delage, MD, Université de Montréal
- Dean A. Fergusson, MHA, PhD, University of Ottawa
- Norbert Froese, MD, University of British Columbia
- Heather Hume, MD, Université de Montréal
- Wendy Lau, MBBS, University of Toronto
- Pierre Robillard, MD, McGill University
- Kathryn Webert, MD, Mc Master University
- Robin K. Whyte, BSc, MB BS, Dalhousie University



Survey Question

Magnetic toys

August 2007

Toys containing small magnets (3–8mm) carry the risk of ingestion or aspiration. If more than one is swallowed, these magnets may connect together from within different segments of the bowel, causing intestinal perforations or obstructions and requiring surgical removal. In 2006, multiple magnet ingestion resulted in the death of a 20-month-old boy in the United States. Since then, hundreds of reports of magnets coming loose from toys were made to the United States Consumer Product Safety Commission and to manufacturers, and approximately 30 more intestinal injuries were identified in the U.S. This led to the North American recall of more than 12 million magnetic toy sets, including Magnetix™ and Polly Pocket™ toys. As well, a number of lawsuits and claims were filed against Magnetix™. Health Canada posted advisories about these toys in June and November 2006.

Although injury and death from these toys have been documented in the U.S., it is unknown whether Canadian health care providers have seen cases of multiple magnet ingestions and whether they are aware of the potential complications. The purpose of this study was to document Canadian data, using a one-time CPSP survey. The goal of the survey was to describe Canadian health care providers' awareness of the risks of multiple magnet ingestion and to describe the number, nature and severity of ingestions reported by participants.

In August 2007, a one-time survey was sent to 2,437 CPSP participants. There were 983 (40%)

respondents and among these, 597 (61%) were aware of the complications of multiple magnet ingestion. Of the participants who were aware of the complications, 49% identified the media as one of their information sources. Clinical experience and Health Canada advisories were identified as information sources, by 26% and 25%, respectively. There were 20 (2%) respondents who had seen multiple magnet ingestions in the preceding year. The majority (88%) of ingestions were seen in children three years and younger. There was wide variability in the products involved and only one multiple magnet ingestion was identified as being caused by a toy that had been recalled. Complications seen varied from none (n=6) to bowel perforation (n=1) and obstruction (n=1). Management varied from observation only (n=5) to endoscopy (n=8), laparotomy (n=4) and admission to the ICU (n=2).

These data document that multiple magnet ingestions are being seen in the Canadian paediatric population, and that these ingestions result in significant morbidity and often require invasive management. With only 61% of respondents being aware of the complications of these ingestions, more effort must be put into educating paediatricians about this hazard.

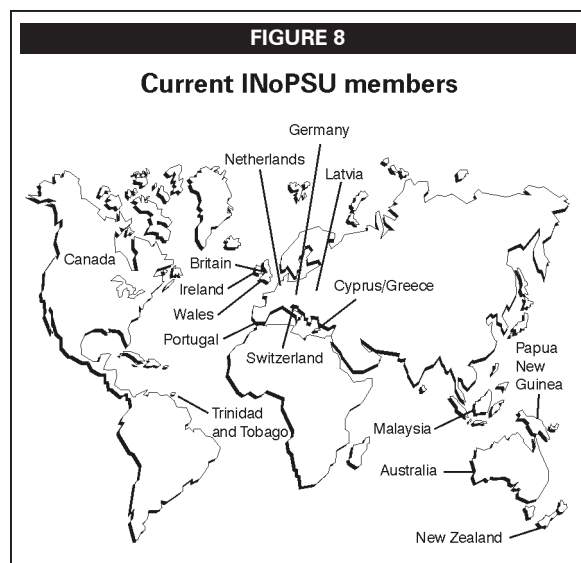
Principal investigators

- Lynne Warda, MD, PhD (Supervisor) and Jennifer D'Mello, MD, University of Manitoba Pediatric Residency Program, AE104-840 Sherbrook St, Winnipeg, MB R3G 2C2; tel.: 204-283-8794; e-mail: jenndmello@yahoo.ca.

International Developments



The International Network of Paediatric Surveillance Units (INoPSU), established in 1998, continues to enhance collaboration between national paediatric surveillance units. INoPSU provides a unique opportunity for simultaneous cross-sectional studies of rare diseases in populations with diverse geographic and ethnic characteristics.



Currently, there are 15 national paediatric surveillance units worldwide that are full members of INoPSU: Australia, Britain, Canada, Germany, Cyprus/Greece, Ireland, Latvia, Malaysia, Netherlands, New Zealand, Papua New Guinea, Portugal, Switzerland, Trinidad and Tobago, and Wales. The British Ophthalmological Surveillance Unit is an associate member.

The network remains active. In 2007, the INoPSU executive launched its e-newsletter (Figure 9), and preparations are well underway for the fifth

INoPSU conference, which will take place in Munich, Germany in 2008.

Further information on all national paediatric surveillance units can be obtained from the INoPSU website at www.inopsu.com.

Highlights from international collaboration

29th National Paediatric Congress, Association des pédiatres de langue française (APLF)

In April 2007, the CPSP participated in the APLF conference with the oral presentation, “*L’impact de la surveillance sur la prévention des blessures: L’expérience canadienne*”. The presentation stimulated interest and discussion.

Pediatric Academic Societies’ 2007 Annual Meeting (PAS/SPR)

In May 2007, the CPSP presented a poster at the PAS/SPR meeting entitled, “International comparison of severe neonatal hyperbilirubinemia and herpes simplex virus infection”. Many participants expressed genuine interest in these issues.

48th Annual Meeting of the European Society for Paediatric Research (ESPR)

In October 2007, the CPSP presented two posters at the ESPR meeting: “International comparison of severe neonatal hyperbilirubinemia and herpes simplex virus infection” and “Impact of surveillance on injury prevention”. Both posters received many inquiries.

TABLE 27

**Studies under surveillance
by national paediatric surveillance units in 2007**

Study	National Paediatric Surveillance Units
Acquired demyelinating syndromes of the central nervous system	CPSP
Acute encephalitis/encephalomyelitis	PPSU
Acute flaccid paralysis	APSU, CPSP, NZPSU, SPSU
Acute rheumatic fever	CPSP, SPSU
Adolescent pregnancy	LPSU
Adrenal insufficiency	IPSU
Adverse drug reactions – serious and life threatening	CPSP
Alcohol intoxication	NSCK
Ambiguous genitals	NSCK
Anaphylaxis	SPSU
Anorexia nervosa	NSCK
Asthma deaths and life-threatening asthma attacks	ESPED
Baby walker injuries	PPSU
Cerebral palsy among five-year-olds	PPSU
Congenital cytomegalovirus infection	APSU, CPSP, PPSU
Congenital myotonic dystrophy	CPSP
Congenital rubella syndrome	APSU, BPSU, NZPSU, SPSU
Congenital toxoplasmosis	CGPSU, PPSU
Craniosynostosis	WPSU
Diabetes mellitus (children five years and less)	ESPED, PPSU
Down's syndrome	NSCK
Early-onset eating disorders	BPSU
Epistaxis in infancy	WPSU
Fetal alcohol syndrome	NSCK
Feto-maternal alloimmune thrombocytopenia (FMAIT)	BPSU
Gallstones in childhood	WPSU
Genital herpes under 11 years presenting to secondary care	BPSU
<i>Haemophilus influenzae</i> invasive infections (all types)	ESPED
Head injuries secondary to suspected child maltreatment (abuse or neglect)	CPSP
Hemoglobinopathy	NSCK
Hemolytic uremic syndrome	CGPSU, NZPSU, PPSU, SPSU
Hemorrhage after adenoidectomy/ tonsillectomy needing treatment	ESPED
Hepatitis C virus infection	APSU
HIV/AIDS	APSU, BPSU, NZPSU
Hodgkin's lymphoma	LPSU
Idiopathic intracranial hypertension	BPSU
Inborn errors of metabolism	NZPSU
Influenza	APSU, ESPED
Intussusception in childhood	APSU, ESPED
Group B streptococcus sepsis	APSU, PPSU
Juvenile dermatomyositis	ESPED

Juvenile idiopathic arthritis	CPSP
Juvenile myoclonic epilepsy	WPSU
Kawasaki disease	PPSU
Kernicterus	CPSP
Leukemia	LPSU
Long-term ventilation	WPSU
Malaria	BPSU
Measles complications	ESPED
Medium-chain acyl-CoA dehydrogenase deficiency	BPSU, CPSP
Methicillin resistant <i>Staphylococcus aureus</i> (MRSA)	BPSU
Morbid obesity	NSCK
Multiple sclerosis	NSCK
Neonatal herpes simplex virus infection	APSU, BPSU, SPSU
Neonatal hyperbilirubinemia – severe	SPSU, NSCK
Neonatal sinus venous thrombosis	ESPED
Neural tube defects	SPSU
Neuroborreliosis	NSCK
Neuromuscular disorders of childhood	APSU
Non-bacterial osteitis	ESPED
Non-cystic fibrosis bronchiectasis	IPSU
Non-Hodgkin's lymphoma	LPSU
Non-tuberculosis mycobacterial infection	APSU
Non-type 1 diabetes mellitus	CPSP, LPSU
Peanut allergy	IPSU
Pertussis	SPSU
Pneumococcal sepsis/meningitis	ESPED, NZPSU
Progressive intellectual and neurological deterioration (PIND)	BPSU
Rett syndrome	APSU
Scleroderma	BPSU
Severe bronchiolitis requiring ICU care	IPSU
Severe combined immunodeficiency	CPSP
Severe seatbelt injuries	APSU
Shaken baby syndrome	ESPED, SPSU
Small intestine insufficiency	NSCK
Subdural hemorrhage	NZPSU
Transfusion-related acute lung injury	CPSP
Varicella (neonatal, congenital, and complications)	APSU, NSCK
Varicella/zoster	IPSU, PPSU
Vitamin D deficiency rickets	APSU, IPSU, WPSU
Vitamin K deficiency bleeding/HDNB	APSU, BPSU, NZPSU, SPSU

Legend:

APSU	Australian Paediatric Surveillance Unit
BPSU	British Paediatric Surveillance Unit
CGPSU	Cyprus/Greece Paediatric Surveillance Unit
CPSP	Canadian Paediatric Surveillance Program
ESPED	German Paediatric Surveillance Unit
IPSU	Irish Paediatric Surveillance Unit
LPSU	Latvian Paediatric Surveillance Unit
NSCK	Netherlands Paediatric Surveillance Unit
NZPSU	New Zealand Paediatric Surveillance Unit
PPSU	Portuguese Paediatric Surveillance Unit
SPSU	Swiss Paediatric Surveillance Unit
WPSU	Welsh Paediatric Surveillance Unit

Highlights from other national paediatric surveillance units

Australia

At the request of the Department of Health and Ageing (DoHA), the Australian Paediatric Surveillance Unit (APSU) conducted emergency surveillance for severe complications of influenza after several child deaths attributed to influenza were reported. Weekly reporting, using a separate influenza report card, began 10 days after the initial call from DoHA. The card and questionnaire return rates were 93% and 88%, respectively. Australian paediatricians are congratulated on their swift response to this short-term emergency surveillance study.

Britain

The past year has seen several British Paediatric Surveillance Unit (BPSU) studies highlighted in the press, particularly the early-onset eating disorder (EOED) study. This study brought to the attention of the press and public the high number of younger children being treated for eating disorders such as anorexia nervosa. This was the first-ever study to involve child and adolescent psychiatrists. Data from this study are currently being compared with data from the APSU and CPSP surveys, and it is hoped that an international comparative paper will result. Interest in the methodology used in the study was such that the child and adolescent psychiatrists intend to adopt the system to develop their own surveillance system. Two further conditions, conversion disorder and bipolar disorder, have been identified as subjects for potential future studies. Many thanks must go to the APSU, who encouraged the EOED investigators in the UK and offered advice when required. This truly demonstrates the power of INOPSU to develop projects of public health importance.

Germany

In 2007, the German Paediatric Surveillance Unit (ESPED) concluded a study on childhood

herpes zoster infection. Research results confirmed that zoster complications are not that rare and do occur in otherwise healthy children. ESPED saw the publication of an article by V. Grote et al entitled "Immunocompetent children account for the majority of complications in childhood herpes zoster" in *The Journal of Infectious Diseases*.

Netherlands

The Netherlands Paediatric Surveillance Unit (NSCK) conducted two important studies where reported cases were higher than expected; namely, alcohol intoxication in children, with 300 cases in one year, and anorexia nervosa, with 707 cases in two years. The unit also initiated a study on multiple sclerosis and concluded two studies on medium-chain acyl-CoA dehydrogenase deficiency and nephrotic syndrome.

New Zealand

The New Zealand Paediatric Surveillance Unit successfully completed 10 years of surveillance of rare diseases. In 2007, Wilson C et al published an article on "The Failure to Diagnose Inborn Errors of Metabolism in New Zealand: The Case for Expanded Newborn Screening" *N Z Med J* 2007; 120:U2727. The study strongly supports the recent establishment of screening in New Zealand.

Portugal

At the 48th Annual Meeting of the European Society for Paediatric Research, the Portuguese Paediatric Surveillance Unit (PPSU) presented on "Epidemiology of cerebral palsy in Portugal among five-year-old children in 2006" and "Validation of assessment scales for communication and oro-motor control of children with cerebral palsy".

Switzerland

In 2007, the Swiss Paediatric Surveillance Unit (SPSU) concluded two studies – neural tube defect and shaken baby syndrome – and initiated one on anaphylaxis. Interestingly, the SPSU ran a first study on hemorrhagic disease of the newborn (vitamin K deficiency bleeding) between 1995 and 2000 and found a higher incidence rate than reported in the literature. The recommendations from this study led to the implementation of a new policy on vitamin K oral regimen prophylaxis. The

SPSU is currently conducting a follow-up study scheduled to run from 2005 to 2011.

Wales

Epidemiology of septo-optic dysplasia was studied in Wales and involved all paediatricians and paediatric ophthalmologists. The study indicated a prevalence of 2.9 per 100,000 children. All had visual impairment ranging from mild to blindness.

The presenting feature in 75% of the cases was the absence of fixing and following (first noticed by the parents). MRI and endocrine abnormalities were found in 65%. Endocrine abnormalities evolved at a varying pace, with thyroid and adrenal deficiencies appearing first. This shows that investigation of these children is the only way of detecting multiple hormone deficiencies and emphasizes the need for continued follow-up.

FIGURE 9



INoPSU

The International Network of Paediatric Surveillance Units

February 2008

Volume 1, Number 1



In This Issue
INoPSU Launch E-newsletter

Latest INoPSU Publications
Annual report 2006-07
Public Health Impact Paper

New INoPSU studies
UK- Intussusception

Rare disease news
Public EU consultation on rare disease. Have your say
Rare disease day
Interview with Dr Peter Corry

Conferences
INoPSU 11-14th September
ICORD 2008 20-22 May 2008

Comments and Contributions for the next newsletter are welcome

Contact Us
<http://www.inopsu.com>
bpsu@rcpch.ac.uk

INoPSU Launch E-newsletter

Welcome to what we hope will be a regular E-newsletter highlighting the work of INoPSU and identifying other activities relating to paediatric rare disease.

For those not familiar with INoPSU, we were set up in 1998 as a worldwide network to increase the communication between researchers undertaking surveillance of rare paediatric diseases. INoPSU currently consists of 12 national surveillance units across 3 continents from Canada to Australia. It involves 10,000 clinicians covering a child population of 50 million children. Between the existing units the epidemiology of over 150 rare paediatric conditions have been investigated. In 2007 nearly 100 conditions were studied.

Further details on INoPSU is available from its website www.inopsu.com


Rob Pereira
 INoPSU Convenor

Latest INoPSU publications



INoPSU annual report – 2006-7 now out

Beyond Counting Numbers – Public Health Impact of Studies Conducted through National Paediatric Surveillance Units. Grenier D et al. *Arch Dis Child* Jun 2007; 92: 527 - 533

- **New INoPSU studies**
UK – Intussusception. First UK paediatric surveillance to involve paediatric surgeons as well as paediatricians.
- **Rare disease News**
Public Consultation regarding a European Action in the Field of Rare Diseases. Have your say in this EU consultation process. [For more information](#)
First European "Rare Disease Day" 29th February 2008. Visit the [website](#) for further details and activities in your country.
Increasing prevalence of rare diseases amongst Bradford England's Pakistani population – OrphaNews Europe interview Dr Peter Corry.
- **Conferences**
INoPSU - To be held in Munich September 11-14th 2008. For further details contact bpsu@rcpch.ac.uk
ICORD 2008: 4th International Conference on Rare Diseases and Orphan Drugs 20-22 May 2008, Washington D.C., USA. For more information: www.icord.se

If you have any comments about this newsletter or would like to contribute something to the next newsletter email bpsu@rcpch.ac.uk

INoPSU E-newsletter

RESEARCH OPPORTUNITIES

Call for New Studies

Wanted

Investigators to initiate new CPSP studies

The program

- Well-established, timely and cost-effective
- Multi-faceted surveillance, capable of collecting reliable data in a variety of fields
- Effective at monitoring low-frequency, high-impact diseases and conditions

Track record

- 80% response from more than 2,500 paediatricians
- 93% data completion rate
- Satisfactory duplicate reporting rate (11%) assuring case ascertainment and participant commitment

Study ideas

A recent survey of paediatricians identified many potential areas for study, including:

Biliary atresia	Heavy metal poisoning
Brachial plexus injury	Hyperthyroidism
Childhood tuberculosis	Imported malaria
Circumcision complications	Kawasaki disease
Complications of measles	Neonatal listeria infections
Congenital adrenal hyperplasia	Rett syndrome
Conversion disorder	Severe hyponatremia or hyponatremia
Familial melanoma	Severe iron-deficiency anemia

If you are interested in these or other studies, or for more program information, please contact 613-526-9397 ext. 239 or e-mail cpssp@cps.ca

"For rare or infrequent events, the CPSP methodology is one of the most useful means of data capture. A unique attribute of this approach is the established credibility of the CPSP with respondents, which enhances both the frequency and quality of replies."

Dr. Richard Stanwick, Chief Medical Health Officer, Vancouver Island Health Authority, and past chair, CPSP Steering Committee.



**For more information on the
Canadian Paediatric Surveillance Program
or a French version of this report,
please contact:**

Canadian Paediatric Society

Louise Painchaud, CPSP Senior Coordinator
2305 St. Laurent Blvd.
Ottawa ON K1G 4J8
Tel.: 613-526-9397, ext. 239
Fax: 613-526-3332
cpasp@cps.ca; www.cps.ca/cpsp

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