



CPSP

CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM



2005 RESULTS



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.

Public health impacts of CPSP studies

1996 to 2005

"It is an important mechanism for surveillance of human health and well-being of one of the most vulnerable populations in Canada, our children. The CPSP has done very well in regard to its current objectives."

Robert McMurtry, MD, Professor of Surgery, University of Western Ontario

"We were struck that such an inexpensive program could have such Canada-wide support from paediatricians. It is a good mechanism for finding low-frequency, high-impact conditions that otherwise would be quite difficult to identify."

Margaret Berry, MD, Neonatologist, The Montreal Children's Hospital

During 10 years of surveillance, the CPSP participants have reported a total of 2,816 confirmed cases. Important public health impacts of study results are illustrated below.

1996 Congenital rubella syndrome

Findings: Rare with 10 cases over 10 years, mostly in non-immunized women

Public health impact: Need to maintain universal and targeted immunizations

1997 Acute flaccid paralysis

Findings: Documentation that Canada is polio-free

Public health impact: Obligation to report to the WHO polio eradication program

1998 Subacute sclerosing panencephalitis

Findings: Rare with two cases over four years

Public health impact: Need to maintain universal immunization against measles and rubella

1999 Cerebral edema in diabetic ketoacidosis (DKA)

Findings: High mortality rate of 23%

Public health impact: Prevention of DKA remains key, as cerebral edema is already present before initiation of therapy

2000 Hemorrhagic disease of the newborn

Findings: Very low rate of 0.22 per 100,000 live births

Public health impact: Supports CPS statement for intramuscular vitamin K as the gold standard

2001 Necrotizing fasciitis (NF)

Findings: Varicella was the most frequent factor of Group A streptococcal-related NF

Public health impact: Supports National Advisory Committee on Immunization statement for universal childhood varicella immunization

2002 Neonatal herpes simplex virus (HSV) infection

Findings: Significant mortality rate of 15.5%

Public health impact: Majority of cases being HSV-1 reinforces need for an HSV-1 and HSV-2 effective vaccine

2003 Vitamin D deficiency rickets

Findings: Over 100 children identified, majority were darker skinned and exclusively breast fed

Public health impact: Supports CPS statement for vitamin D supplementation of all exclusively breast-fed children

2004 Baby walkers

Findings: Confirmation that injuries are still occurring

Public health impact: Contributed to Health Canada's mandatory total ban on baby walker sales in April 2004

2004 Infant bath seats

Findings: Confirmation of injuries and drownings

Public health impact: Supported Health Canada's advisory on drowning hazard of infant bath seats in April 2005

2005 Lap-belt syndrome

Findings: High morbidity with 25% of children left paraplegic

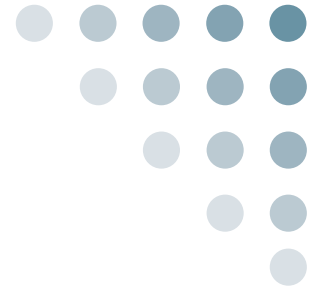
Public health impact: Supports CPS advocacy that all provinces/territories adopt proper child restraints in motor vehicles and booster seat legislation





Table of Contents

Acknowledgements	3
Foreword	4
President of the Canadian Paediatric Society	4
CPSP Chairman	5
CPSP Steering Committee	6
CPSP Working Group	6
Publications in 2005	7
Published papers related to studies	7
Highlights published in <i>Paediatrics & Child Health</i>	7
Presentations in 2005	8
National	8
International.....	8
Funding	9
Surveillance at Work	10
Overview	10
Investigators' corner	12
Studies timeline.....	13
CPSP Principal Investigators	14
Surveillance Studies in 2005	15
Acquired demyelinating syndromes of the central nervous system	15
Acute flaccid paralysis	18
Acute rheumatic fever.....	22
Adverse drug reactions – serious and life-threatening.....	24
Congenital cytomegalovirus infection.....	27
Congenital myotonic dystrophy	30
Early-onset eating disorders (final report)	32
Head injury secondary to suspected child maltreatment (abuse or neglect)	35
Lap-belt syndrome (final report)	38
Medium-chain acyl-coenzyme A dehydrogenase deficiency	40
Osteogenesis imperfecta (final report)	42
Severe combined immunodeficiency.....	45
Transfusion-related acute lung injury.....	47
New Studies in 2006	49
Kernicterus	49
Non-type 1 diabetes mellitus.....	50
Survey Questions	51
Adolescent depression and side effects of selective serotonin reuptake inhibitors	51
Congenital cytomegalovirus infection.....	52
International adoption	53
International Developments	54
Highlights from other national paediatric surveillance units	55
Research Opportunities – Call for New Studies	inside back cover



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.

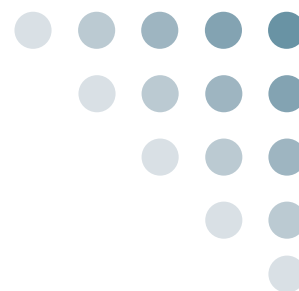
For their role in the verification of data collected, we thank:

- Canadian Association of Paediatric Health Centres
- Canadian Institute for Health Information
- Canadian Paediatric Decision Support Network
- IMPACT (Immunization Monitoring Program ACTive) centres

We also gratefully acknowledge the financial support received to maintain and expand the program. A summary of supporters is found on page 9 in this report.

The partnership between the Canadian Paediatric Society (CPS) and the Public Health Agency of Canada (PHAC) has allowed the CPSP to grow in Canada and to take a leadership role on the international scene. We recognize and thankfully acknowledge this historical support.

Foreword



President of the Canadian Paediatric Society



Dr. Denis Leduc

After a decade of successful active surveillance, one realizes that for most rare diseases affecting children and youth, the epidemiological data are either non-existent or inadequate. Well established and recognized both nationally and internationally, the CPSP is now in a favourable position to advance research and provide invaluable results that will guide paediatricians and public health policy makers.

A good example is the lap-belt syndrome study that showed 25% of children with this type of motor vehicle injury were left paraplegic. The CPS, with others, is advocating on the importance of proper child restraint in motor vehicles and the use of booster seats. In June 2005, the CPS published a report entitled, *Are We Doing Enough? A status report on Canadian public policy and child and youth health*, which reviews the adequacy of laws to protect the health and safety of children. The report includes a grading of each province and territory on its booster seat law. In September 2005, a new child car seat and booster seat law went into effect in Ontario that meets all of the CPS recommendations. Advocacy efforts will continue until all jurisdictions have complied.

The program is pleased to see experienced faculty members mentoring young researchers with their study proposals and will further pursue this avenue. Another evolving phenomenon is for CPSP studies to represent the epidemiological component of major research endeavours, such as the acquired demyelinating syndromes of the central nervous system study and multiple sclerosis research, as well as the congenital myotonic dystrophy study.

In the future, the CPSP will be looking at alternate sources of ascertainment to further improve the number of cases reported and will continue to contribute to the work of the International Network of Paediatric Surveillance Units.

CPSP achievements have been made possible because of the dedication of participants who faithfully complete their report forms every month. I would like to sincerely thank all of them for making the CPSP work.

Happy tenth anniversary to the CPSP! We look forward to a promising future.

CPSP Chairman



Dr. Gilles Delage

A decade of paediatric surveillance

As the CPSP is turning 10 years old, this is an opportune time to reflect on a decade of surveillance. What are some of the achievements to date? Where does the CPSP stand on the international front? What are the priorities for the future?

The CPSP research results reinforced the astuteness of many CPS recommendations with important repercussions such as the following:

- Vitamin K administration to all newborns to prevent hemorrhagic disease of the newborn
- Vitamin D supplementation to all exclusively breast-fed newborns to prevent vitamin D deficiency rickets
- Universal rubella immunization and catch-up immunization of all rubella susceptible mothers in the immediate postpartum period to prevent congenital rubella syndrome
- Universal varicella immunization to prevent complications such as group A streptococcus-related necrotizing fasciitis
- Evaluations of all newborns within 48 hours of early discharge to ensure early detection of hyperbilirubinemia and the prevention of kernicterus
- Total ban of baby walkers to prevent injuries
- Public health warning to alert parents of the risks of unsupervised use of infant bath seats
- Mandatory use of appropriate child restraint in motor vehicles, including prolonged use of booster seats to prevent lap-belt syndrome

The CPSP is also very well known and respected on the international scene. The CPSP is an active member of the International Network of Paediatric Surveillance Units (INoPSU) and promotes collaboration and cooperation among surveillance units and investigators. In June 2000, the program hosted the inaugural meeting of INoPSU in Ottawa, providing an open forum for discussion and the opportunity to share information. Following an invitation by the Argentinean Paediatric Society, CPSP representatives had the privilege of working with colleagues to create a Perinatal Network in Buenos Aires in 2004.

One of the many challenges ahead is to secure funding for the long-term continuation of the CPSP, including the establishment of an annual bursary to encourage young researchers. Another important priority is developing a method for rapid surveillance in case of a public health emergency, including the option of web-based reporting. The CPSP is ready to face these challenges.

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
Dr. Rick Cooper	Paediatric Chairs of Canada
Ms. Marie Adèle Davis	Canadian Paediatric Society
Ms. Jo-Anne Doherty	Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada
Dr. Kevin Gordon	Canadian Association of Child Neurology (Liaison)
Dr. Danielle Grenier	Canadian Paediatric Society
Dr. Richard Haber	Canadian Paediatric Society
Dr. Bryce Larke	Canadian Paediatric Society
Dr. Simon Levin	Canadian Association of Child Neurology (Liaison)
Dr. Catherine McCourt	Centre for Healthy Human Development, Public Health Agency of Canada
Mr. Paul Muirhead	Consultant
Dr. Jeff Scott	Council of Chief Medical Officers of Health (Liaison)
Ms. Sarah Srikanthan	Canadian Paediatric Society
Dr. Theresa Tam	Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada
Dr. Wendy Vaudry	IMPACT (Immunization Monitoring Program ACTIVE) (Liaison)
Dr. Lynne Warda	Canadian Paediatric Society
Dr. Lonnie Zwaigenbaum	Canadian Paediatric Society

CPSP Working Group

Ms. Sarah Srikanthan (Chair)	Canadian Paediatric Society
Ms. Marie Adèle Davis	Canadian Paediatric Society
Ms. Jo-Anne Doherty	Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada
Dr. Danielle Grenier	Canadian Paediatric Society
Dr. Catherine McCourt	Centre for Healthy Human Development, Public Health Agency of Canada

Publications in 2005



Published papers related to studies

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

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

Highlights published in *Paediatrics & Child Health*

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

Canadian Paediatric Surveillance Program 2005 quiz. *Paediatr Child Health* 2005;10(10):590,601,608

The challenge of severe infections in infancy. *Paediatr Child Health* 2005;10(9):567

Fragile bones or child maltreatment? *Paediatr Child Health* 2005;10(8):500

Does anorexia nervosa occur in the prepubertal years? *Paediatr Child Health* 2005;10(7):378

Congenital cytomegalovirus infection: What is the best way to make the diagnosis? *Paediatr Child Health* 2005;10(6):IBC

Helping newborns to a healthy start: Clinical impact of your Canadian Paediatric Surveillance Program monthly feedback. *Paediatr Child Health* 2005;10(5):268

Human growth hormone therapy in Prader-Willi syndrome. *Paediatr Child Health* 2005;10(4):202

A simple sore throat ... or not? *Paediatr Child Health* 2005;10(2):94

Infant bath seat survey: Results and next steps. *Paediatr Child Health* 2005;10(1):27

Presentations in 2005

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

National

Incidence and cohort study of congenital DM. Campbell C, Levin S, Jacob P, Siu V, Venance S. Presented at the 5th International Myotonic Dystrophy Consortium Meeting (IDMC-5), Quebec City, October 2005.

Lessons from Prader-Willi syndrome (PWS): Integrating weight and behavior management. Forster JL, Berall G, Gourash LM. Presented at the 52nd Annual Meeting of the American Academy of Child and Adolescent Psychiatry, Toronto, October 2005.

Prader-Willi syndrome (preliminary partial results). Berall G. Presented at the Come to Your Senses Conference, Toronto, October 2005.

Early recognition of MS in paediatrics: ADEM. Banwell B. Presented at the 82nd Annual Conference of the Canadian Paediatric Society, Vancouver, June 2005.

Severe neonatal hyperbilirubinemia in Canadian newborns: A preventable disease? Campbell DM, Shah V, Sgro M. Presented at the 82nd Annual Conference of the Canadian Paediatric Society, Vancouver, June 2005.

One-time surveys: CPSP added value. Grenier D, Medaglia A, Srikanthan S. Presented at the 82nd Annual Conference of the Canadian Paediatric Society, Vancouver, June 2005.

Surveillance: Helping newborns get off to a good start. Sgro M, Wong T. Presented at the 82nd Annual Conference of the Canadian Paediatric Society, Vancouver, June 2005.

Feeding in CHARGE syndrome. Dobbeltsteyn C, Crist B, Blake KD, Rashid M. Presented at the CHARGE Syndrome Canada Junefest 2005, Toronto, June 2005.

Acquired demyelination in children. Banwell B. Presented at various paediatric grand rounds and specialty rounds in Hamilton, Kingston, London, Mississauga, Ottawa, and Vancouver in 2005.

Paediatric surveillance: A research asset. Grenier D, Medaglia A, Srikanthan S. Presented at paediatric grand rounds in Edmonton, Ottawa, and Kingston in 2005.

International

Active surveillance of early-onset eating disorders, vitamin D deficiency rickets, and Prader-Willi syndrome. Doherty J, Grenier D, Pinhas L, Berall G, Ward L, Srikanthan S. Presented at the 46th Annual Meeting of the European Society for Paediatric Research, Siena, Italy, September 2005.

Prospective study of the clinical epidemiology, pathobiology, and neuroimaging features of Canadian children with clinically isolated demyelinating syndromes: methodology and preliminary incidence data. Banwell B, Bar-Or A, Arnold D, Sadovnick D, Kennedy J. Presented at the 10th Annual Meeting of the Americas Committee for Treatment and Research in Multiple Sclerosis, Thessaloniki, Greece, September 2005.

Lap-belt syndrome (results of the first 18 months of study). Cyr C. Presented at the 9th Congress of the World Federation of Societies of Intensive and Critical Care Medicine, Buenos Aires, Argentina, August 2005.

Prader-Willi syndrome (preliminary results). Desantadina V. Presented at the IV Latin-American PWS Conference, Buenos Aires, Argentina, May 2005.

Campbell DM, Shah V, Sgro M. Severe neonatal hyperbilirubinemia in Canadian newborns – A preventable disease. Presented at the SPR/PAS Annual Meeting, Washington, DC, May 2005.

A study of feeding difficulties in children with CHARGE syndrome. Dobbeltsteyn C, Crist B, Blake KD, Rashid M. Presented at the Great Lakes Regional Conference for Child Health, Columbus, Ohio, April 2005.

Funding



Funding for the CPSP is required for program management, including administrative and financial support. The surveillance program is funded through a combination of government funds and unrestricted grants from Canadian charities, research institutions, hospitals and corporations. All funding is provided to support the program, not an individual study.

We gratefully acknowledge the following organizations that provided funding to the CPSP during part or all of 2005.

Government departments

Health Canada

- First Nations and Inuit Health Branch
 - Office of Community Medicine
- Health Products and Food Branch
 - Marketed Health Products Directorate
 - Policy and Partnerships Division
 - Office of Nutrition Policy and Promotion
 - Food and Nutrition Surveillance

Public Health Agency of Canada

- Centre for Healthy Human Development
 - Division of Childhood and Adolescence
 - Health Surveillance and Epidemiology Division
 - Healthy Communities Division
- Centre for Infectious Disease Prevention and Control
 - Immunization and Respiratory Infections Division

Transport Canada

- Safety and Security Group
 - Road Safety and Motor Vehicle Regulation

Non-governmental sources

- Abbott Laboratories Ltd.
- Bristol-Myers Squibb Company
- Children's Health Research Institute (Children's Hospital of Western Ontario)
- Children's Hospital of Eastern Ontario
- Children's Hospital of Eastern Ontario Research Institute
- Department of Psychiatry, Sunnybrook and Women's College Health Sciences Centre
- Hema-Quebec
- IWK Health Centre
- Janeway Children's Hospital Foundation
- Lawson Health Research Institute
- Merck Frosst Canada Ltd.
- Multiple Sclerosis Scientific Research Foundation
- Ontario Neurotrauma Foundation Prevention Committee
- Quebec Foundation for Research into Children's Diseases
- Shriners Hospital Board of Governors
- William Singeris National Centre for Myotonic Dystrophy
- Wyeth-Ayerst Canada Inc.

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. 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 reporting form. The full process is summarized in Figure 1 and includes the 3Ds of surveillance: detection, deduction and dissemination.

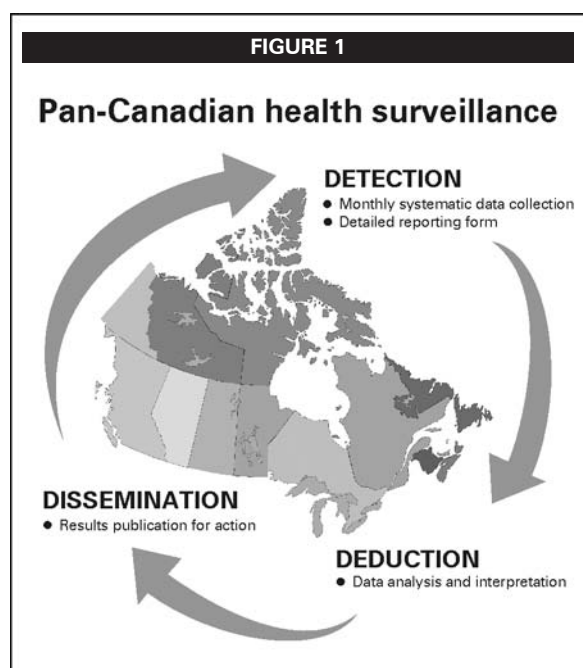
Reporting

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.

Only non-nominal patient information, such as the date of birth, sex of the child and comments on the condition, is requested for each reported case. This anonymous information is used to exclude duplicates and is sent to the original respondent to request case-specific information. Once the detailed report 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.

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 82% national reporting rates (see Table 1 for details) and the 93% response rate for completion of detailed questionnaires (see Table 2 for study breakdown).

TABLE 1

**Initial response rates (%)
and number of participants for 2005**

Province/territory	Reporting rates (%)	Number of participants
Alberta	84	268
British Columbia	80	258
Manitoba	82	124
New Brunswick	80	32
Newfoundland and Labrador	91	43
Nova Scotia	88	92
Northwest Territories	100	3
Nunavut	100	1
Ontario	82	960
Prince Edward Island	93	7
Quebec	77	664
Saskatchewan	75	46
Yukon	89	2

TABLE 2

**2005 detailed questionnaire completion rates
as of March 1, 2006**

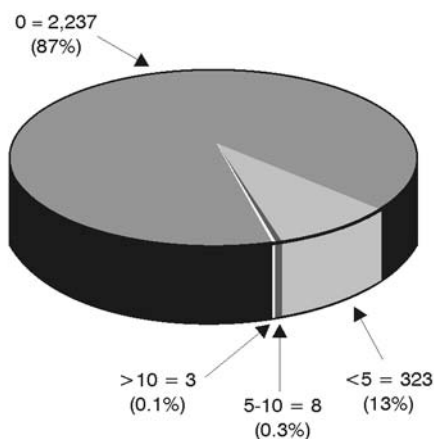
Studies/conditions	Reported cases	Pending	% Completion rate
Acquired demyelinating syndromes of the central nervous system	112	6	95
Acute flaccid paralysis	73	2	97
Acute rheumatic fever	39	1	97
Adverse drug reactions – serious and life-threatening	74	12	84
Congenital cytomegalovirus infection	39	3	92
Congenital myotonic dystrophy	25	0	100
Early-onset eating disorders	16	0	100
Head injury secondary to suspected child maltreatment (abuse or neglect)	111	13	88
Lap-belt syndrome	9	1	89
Medium-chain acyl-coenzyme A dehydrogenase deficiency	3	1	67
Osteogenesis imperfecta	28	2	93
Severe combined immunodeficiency	20	0	100
Transfusion-related acute lung injury	0	0	100
Total number of cases (all studies)	549	41	93

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 2005, the majority of participants (87%) 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 2005.

FIGURE 2

**Number of cases reported
by respondents in 2005**



As studies come and go, the workload shifts to different subspecialties. The 2005 studies with the most reports were acquired demyelinating syndromes of the central nervous system 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 the Steering Committee's insistence on short, precise and pertinent detailed questionnaires.

To thank paediatricians and paediatric subspecialists for their tremendous commitment and support, 1,742 personal certificates were sent to acknowledge CPSP participation in 2005 and

310 letters of thanks went to participants who reported a case in 2005. In addition, Drs. Peter J. Azzopardi (ON) and Margaret Choi (BC) 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 2006 CPS Annual Conference in St. John's were Dr. Cheri L. Deal (QC), who responded for all months in 2005, and Dr. Kristi D. Zinkiew (BC), who completed and returned a questionnaire for a reported case.

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 2,570 participants. The program is committed to a high case ascertainment rate of over 90% and, due to follow-up reminders to non-responders, boasts a high response rate of 93% on detailed reports (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 well-being 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 public health importance or 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 Web site 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 2005 one-time survey questions on adolescent depression and side effects of selective serotonin reuptake inhibitors, congenital cytomegalovirus infection, and international adoption are found on pages 51, 52 and 53.

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

Studies timeline

TABLE 5
CPSP studies timeline (by end date)

Studies	Start date	End date	Total confirmed cases to December 31, 2005
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	203
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
Congenital cytomegalovirus infection	March 2005	February 2007	18
Head injury secondary to suspected child maltreatment (abuse or neglect)	March 2005	February 2007	43
Acquired demyelinating syndromes of the central nervous system	April 2004	March 2007	135
Acute rheumatic fever	April 2004	March 2007	38
Non-type 1 diabetes mellitus	April 2006	March 2007	N/A
Severe combined immunodeficiency	April 2004	March 2007	12
Medium-chain acyl-coenzyme A dehydrogenase deficiency	September 2005	August 2007	1
Transfusion-related acute lung injury	September 2005	August 2007	0
Acute flaccid paralysis	January 1996	December 2007	415
Adverse drug reactions – serious and life-threatening	January 2004	December 2007	86
Congenital myotonic dystrophy	March 2005	February 2008	4
Kernicterus	September 2006	August 2008	N/A

CPSP Principal Investigators



Surveillance studies in 2005



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



Jeannette Macey
Acute flaccid paralysis



Dr. Christina Templeton
Acute rheumatic fever



Dr. Bruce Carleton
Adverse drug
reactions – serious
and life-threatening



Dr. Wendy Vaudry
Congenital
cytomegalovirus
infection



Dr. Craig Campbell
Congenital myotonic
dystrophy



Dr. Leora Pinhas
Early-onset eating
disorders



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



Dr. Claude Cyr
Lap-belt syndrome



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

New studies in 2006



Dr. Leanne Ward
Osteogenesis
imperfecta



Dr. Ezzat Farzad
Severe combined
immunodeficiency



Dr. France Gauvin
Transfusion-related
acute lung injury



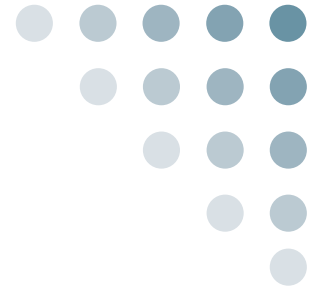
Dr. Shazhan Amed
Non-type 1 diabetes
mellitus



Dr. Michael Sgro
Kernicterus



Surveillance Studies in 2005



Acquired demyelinating syndromes of the central nervous system

April 2004 to March 2007

Highlights

- Demyelination is not as rare as previously thought, as 83 cases were confirmed in 2005.
- Eight confirmed cases developed multiple sclerosis.
- Nearly all of the 83 children with demyelination (87%) required treatment and 100% had a brain MRI performed.
- Reporting physicians discussed the possibility of recurrent demyelination with patients and families in 89% of first-time cases.

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 our 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 will gather case-specific data to document the clinical features, epidemiological characteristics, familial autoimmune profile and the current medical care practices provided to children with ADS. This initiative will provide a measure of the impact of CNS demyelination on Canadian children and aims to enhance the care of affected children by increasing awareness among Canadian

paediatricians of CNS demyelination, particularly MS, and 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; and/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 83 confirmed cases of demyelination reported in 2005. The majority of them were from Ontario (44%), British Columbia (16%), Alberta (14%), Quebec (12%) and Manitoba (6%). Three other provinces accounted for the remaining confirmed ADS cases. The mean age was 10.7

years (range 0.7–17.9 years) and the female to male ratio was 1.1:1 (47 females, 44 males).

TABLE 6

**Acquired demyelinating syndromes
of the central nervous system cases in 2005**

Reported	Duplicates	Excluded	Under review	Confirmed
108	12	3	10	83

Epidemiological and familial autoimmune data

Most of the confirmed cases in 2005 were born in Canada (95%, 79 cases) and four were born outside North America (Philippines, Sri Lanka, Syria, Saudi Arabia). The majority of the patients reported European ancestry (46%). Other ancestries included Asian (20%), Middle Eastern (3%), Aboriginal (8%), Central and South American (9%), Caribbean (1%) and mixed-ancestry (11%).

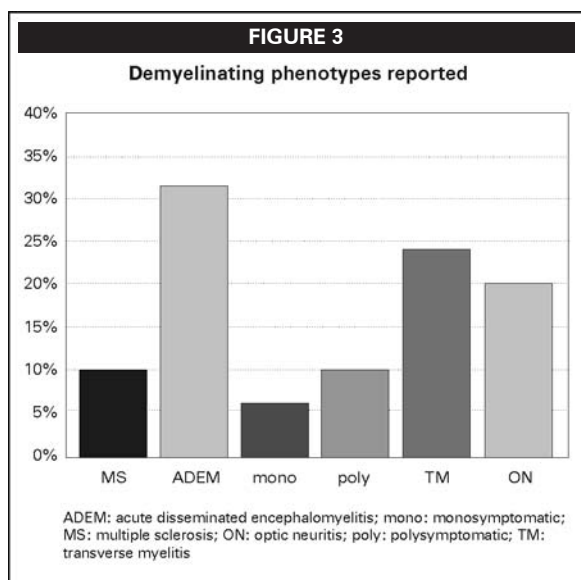
Eight percent (8%, 7) of the 83 confirmed cases reported a family history of MS.

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 (31%), followed by cases of transverse myelitis (24%), optic neuritis (20%), polysymptomatic (10%) and monosymptomatic (6%). Of the 17 optic neuritis cases, nine were documented as unilateral and seven were bilateral. One child with transverse myelitis had a concurrent diagnosis of systemic lupus erythematosus.

Treatment with corticosteroids or immune globulin for the demyelinating event was required for nearly all cases (87%). Combinations of corticosteroids and immune globulins were necessary for eight patients.

Brain MRIs were performed in all of the 83 confirmed cases and 67 (80%) reported abnormal white matter changes. Eighty-eight percent (88%) of the confirmed cases were first-time acute demyelinating syndromes and the risk of recurrent demyelination was discussed with the patients and families in 89% of cases.



Conclusion

On average, approximately six cases were reported per month in the first nine months of this study (April 1 to December 31, 2004). This rate of reporting increased slightly to seven cases per month in the second year of the study (January 1 to December 31, 2005), likely due to increased awareness. 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 data collected through this surveillance study approaches the above estimate and indicates that the incidence of ADS is nearly 85 cases per year.

The distribution of cases reported in each province has changed from 2004 to 2005. In 2005, reporting

more than doubled in Quebec and tripled in British Columbia when compared to 2004. The reports from Alberta increased from 0 cases in 2004 to 12 cases in 2005. The total number of cases reported in Ontario was 37 in 2004 and 2005; however, Ontario accounted for 70% of the total reports in 2004 and 44% in 2005. The increased proportion of confirmed cases among all provinces may reflect an increased awareness of this project and greater recognition of paediatric demyelination across Canada.

The majority of patients required treatment for their demyelinating event and all confirmed cases underwent brain MRI imaging. The proportion of children undergoing MRI has increased from 87% in 2004 to 100% in 2005. This may relate to increased understanding and awareness of MRI as a diagnostic tool in demyelination.

For all children with ADS, there is a risk of recurrent demyelination (MS). The data from this study indicate that this risk is being discussed with patients and families, demonstrating Canadian paediatricians are aware of this MS risk in most children presenting with ADS.

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Acute flaccid paralysis

January 1996 to December 2007

Highlights

- Over the past five years, AFP detection rates have been below expected targets.
- Duplicate reporting rates are high, suggesting there is good sensitivity in monitoring.
- The risk of wild poliovirus importation into Canada remains, due to ongoing transmission in endemic and newly reinfected countries.
- Stool testing is essential to rule out poliovirus infection.
- AFP surveillance is a World Health Organization recommended activity for documenting Canada's polio-free status.

Background

Elimination of indigenous wild poliovirus transmission in Canada, and the rest of the American region, was certified in September 1994. Maintaining vigilance in the absence of disease is a challenge. However, until global eradication of poliomyelitis is achieved, there is an ongoing risk of wild poliovirus importation. Outbreaks of polio are presently occurring in several endemic and newly reinfected regions in Africa and Asia. 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 crucial 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 is important to ensure that appropriate investigations are promptly conducted to rule out polio. As well, documentation of monitoring and polio-specific investigations for all AFP cases, regardless of suspected diagnosis, is the means by which Canada is able to maintain its polio-free certification status.

AFP surveillance is conducted jointly through the following two paediatric surveillance networks in Canada: the IMPACT (Immunization Monitoring Program, ACTive) network of paediatric tertiary care centres initiated AFP surveillance in 1991; and the CPSP began supplementing AFP monitoring and investigation activities in 1996. This report presents the results of AFP surveillance in 2005, with a comparison to previous years.

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 poliovirus infections. Key objectives, based on World Health Organization (WHO) quality assurance criteria, include the following:

- 1) Detect at least one case of non-polio AFP per year for every 100,000 children less than 15 years of age (57 to 60 AFP cases per year in Canada).
- 2) Collect adequate stool specimens for poliovirus examination from at least 80% of AFP cases within 14 days of the onset of paralysis.
- 3) Conduct 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

There was a total of 46 confirmed cases of AFP during 2005. Of the confirmed cases, 39 were identified initially by the CPSP and another seven cases by IMPACT only. Of the initial notifications from the CPSP, 21 of the detailed reports were submitted from IMPACT sites and the remaining 18 from the CPSP. Confirmed cases were reported from most provinces and may have included cases

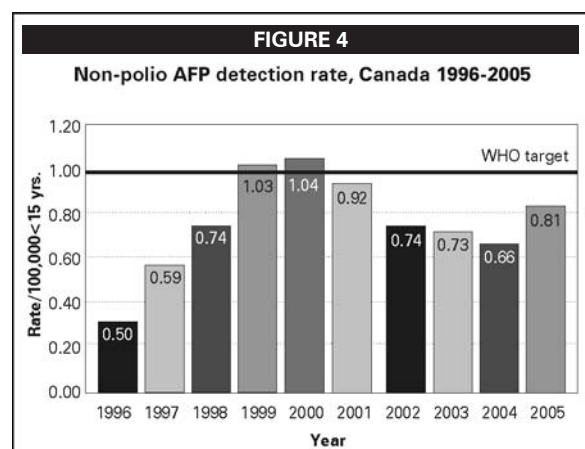
transferred from other provinces or territories into the reporting province. The AFP detection rate ranged from 0.31/100,000 in the Atlantic Provinces to 3.6/100,000 in Manitoba.

TABLE 7

Acute flaccid paralysis cases in 2005

Reported	Duplicates	Excluded	Under review	Confirmed
77	24	7	0	46

Seven reports were excluded: six based on age criteria (for children over 15 years) and one based on initial diagnostic criteria (initial diagnosis of Bell's palsy with no further investigation for AFP). The 46 confirmed cases represent a non-polio AFP detection rate of 0.81/100,000 children under 15 years of age, which is below the 1/100,000 expected rate by more than 10 cases (57 cases expected for 2005). Almost half of the confirmed cases (21 cases, 46%) were captured multiple times by the CPSP and IMPACT. With the anticipated 'late reports' for the current year, the final number of confirmed cases is likely to be somewhat higher but still below the WHO target rate (Figure 4).



In 2005, AFP cases ranged in age from five days to 14 years (median 5.5 years, mean 12.1 years). Table 8 shows the age distribution of AFP cases between 1996 and 2005. The most notable patterns are an increase in the 0–1 year age group and a decrease in the 6–10 year age group occurring after 2000. There is no apparent reason for these patterns but further exploration of possible changes in monitoring activities or disease patterns may reveal an explanation. The male to

female ratio has been variable over the years, with no clear pattern demonstrated. In 2005, there were 2.5 male cases for every female case reported; yet, over the 10 years of surveillance, the ratio ranges from 0.85 to 2.5 males for every female.

Although most Canadian children today are vaccinated against polio, only 22 of the 46 confirmed AFP cases (48%) had detailed documentation of routine childhood immunization. Of these, 21/22 (91%) had received age-appropriate polio immunization. An additional 10 cases had polio vaccination information reported as “up-to-date” but with no accompanying polio vaccine-specific information provided.

TABLE 8

Age distribution of AFP cases reported to the CPSP

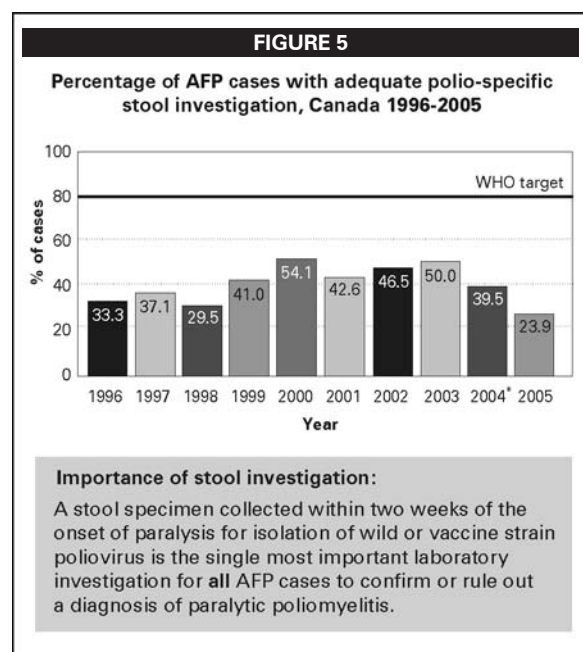
Age group (years)	Number of cases									
	1996	1997	1998	1999	2000	2001	2002	2003	2004*	2005
0–1	2	–	2	3	2	8	10	5	5	8
2–5	11	13	15	18	24	18	16	17	15	15
6–10	9	12	18	23	22	14	11	7	10	12
11–14	8	10	9	17	13	14	6	15	8	11
Total	30	35	44	61	61	54	43	44	38	46

* Includes three delayed reports not included in the CPSP 2004 Results

Virological investigation for polio or other enteroviruses

Virological investigation of AFP cases in 2005 included the collection and testing of stool specimens for 18 cases (39%), cerebrospinal fluid (CSF) for 27 cases (59%), throat swabs for 11 cases (24%) and polio-specific serology for one case (2%). Stool virology was not done or status was unknown for more than half of the cases (54%). Although stool was collected for virological investigation for 18 cases, only 11 (24%) had adequate stool investigation for isolation of poliovirus or non-polio enteroviruses. For the remaining seven cases (15%), although stool specimens were collected, the collection date was either not documented or collection was done after two weeks of the onset of paralysis when virus excretion is decreasing. There were also two instances in which stool collection was done but laboratory testing was reported as not done or

results not received. Overall, rates of adequate stool investigation remain considerably lower than the WHO target of 80% (Figure 5). There was no positive identification of polioviruses from any of the virological investigations.



* Includes three delayed reports not included in the CPSP 2004 Results

Campylobacter investigation

Campylobacter stool culture was added to the AFP surveillance study in 2001 to explore possible links between infection with this bacteria and Guillain-Barré syndrome (GBS). Since then, testing for *Campylobacter* increased from 7% to 53% of cases investigated. In 2005, this dropped to 24%. No tests were positive for *Campylobacter*. Given the short time period and the relatively low number of cases investigated each year, it is not possible to draw any conclusions regarding the possible role of *Campylobacter* infection in the development of GBS.

Neurological investigations

Neurological investigations consisted of one or more of the following: CSF examination (protein, glucose, white blood cells, neutrophils, lymphocytes and red blood cells), nerve conduction studies, electromyography and MRI or CT scan. Abnormal neurological findings compatible with the final neurological diagnosis were reported for one or

more of the tests done. MRI or CT scanning was the most frequently used neurological investigation (33 cases, 72%), showing abnormalities in 20/33 cases (61%). Electromyography and/or nerve conduction studies were the second most frequently used neurological investigations (26 cases, 57%), showing abnormalities in 18/26 cases (69%). CSF chemistry was used least often (10 cases, 22%), showing abnormalities in 9/10 cases (90%).

As observed in previous years, the majority of AFP cases (39 cases, 85%) were diagnosed as either GBS (29 cases, 63%) or transverse myelitis (10 cases, 22%) (Table 9). Of the 29 cases diagnosed as GBS, three were atypical presentations, including one Miller-Fisher variant and two unspecified presentations. The 10 cases of transverse myelitis included two with concurrent diagnoses, one with systemic lupus and one with accompanying acute disseminated encephalomyelitis.

TABLE 9

Neurological diagnosis of AFP cases, Canada 1996-2005

Diagnosis	Number of cases (% of total)									
	1996	1997	1998	1999	2000	2001	2002	2003	2004*	2005
Polio	0	0	0	0	0	0	0	0	0	0
Guillain-Barré syndrome	21 (70.0)	29 (82.8)	34 (77.3)	50 (82.0)	49 (80.0)	42 (77.7)	33 (76.7)	33 (75.0)	27 (71.1)	29 (63.0)
Transverse myelitis	6 (20.0)	2 (5.7)	6 (13.6)	7 (11.5)	4 (6.6)	8 (14.8)	7 (16.3)	4 (9.1)	7 (18.4)	10 (21.7)
Other†	2 (6.6)	3 (8.6)	1 (2.3)	4 (6.6)	8 (13.1)	4 (7.4)	3 (7.0)	7 (16.3)	4 (10.5)	7 (15.2)
Not specified or undetermined diagnosis/etiology	1 (3.3)	1 (2.9)	3 (6.8)	—	—	—	—	—	—	—
Total	30 (100)	35 (100)	44 (100)	61 (100)	61 (100)	54 (100)	43 (100)	44 (100)	38 (100)	46 (100)

* Includes three delayed reports not included in the CPSP 2004 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

Hospitalization and outcome

The majority of AFP cases (42/46, 91%) in 2005 required hospitalization, with lengths of stay ranging from two to 48 days (average 23 days). Outcome at the time of the initial report was documented for 37 cases (80%) including: four cases (9%) fully

recovered, 32 cases (70%) partially recovered with residual weakness or paralysis and one case (2%) outcome pending (not recovered, condition progressive). For the remaining nine cases (20%), outcome status at the time of the initial report was either unknown or not recorded. A key WHO recommended target for high-quality AFP surveillance is follow-up investigation at least 60 days after the onset of paralysis in at least 80% of AFP cases to verify the presence of residual paralysis. Longer-term outcomes were not well documented in 2005. The status at 60 days was documented for only 11 cases (24%), including two cases which were reported as fully recovered at 60 days, six who were partially recovered with residual weakness or paralysis and three with outcomes still pending (i.e., either not recovered or condition progressive).

Conclusion

The 46 AFP cases (0.81/100,000 <15 years) reported to date for 2005 is below the expected number, yet this represents an increase compared to the three previous years. Though Canada met the WHO expected target for non-polio AFP detection in 1999 and 2000, the ten-year average falls below this target at 0.77/100,000 (range 0.50–1.04) or 45 cases. The reasons for the lower than expected detection rate in Canada are not clear. Non-polio AFP detection rates showed an initial improvement from 0.50/100,000 <15 years in 1996 to >1/100,000 <15 years in 1999–2000, but this was followed by a decrease each year from 2001 to 2004. These lower than expected rates may be a result of under-detection of cases; however, duplicate reporting rates are high (46%), suggesting there is good sensitivity in monitoring. Alternatively, they may be a true reflection of lower baseline levels for non-polio AFP in Canada and other developed countries. Likewise, the reasons for the observed trends in the detection rate are also unclear. Changing trends in the detection rate may be related to changes in monitoring and detection or to actual cycles of disease prevalence contributing to AFP. These are areas that require further exploration.

Results from AFP case investigations for the ten-year surveillance period from 1996 to 2005 indicate that, while less than 50% of cases had stool collected for isolation of polioviruses or

non-polio enteroviruses, 80–90% had one or more neurological investigation conducted. Given that most AFP cases in Canada are diagnosed as either GBS or transverse myelitis, clinical signs and symptoms consistent with these conditions may favour neurological investigation. However, the importance of polio-specific stool investigations and other virological investigations should not be minimized, as 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. As well, non-polio viruses that may also cause AFP (e.g., other enteroviruses, such as echoviruses and Coxsackie viruses) can likewise be investigated through prompt virological investigation of stool or other clinical specimens. Negative results of appropriate polio-specific investigations are as important as positive results in AFP case evaluations. Canada could improve the quality of AFP investigations through increased stool sampling and virological testing for polioviruses and non-polio enteroviruses. Likewise, improved documentation of 60-day follow-up with observation of any residual paralysis would increase the quality of AFP surveillance and documentation in Canada. In the meantime, reliable and effective surveillance systems continue to be vital for detecting possible importation of wild and vaccine-derived poliovirus, and AFP surveillance remains an important activity in Canada.

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Acute rheumatic fever

April 2004 to March 2007

Highlights

- Acute rheumatic fever is extremely rare in the paediatric population.
- Affected children have significant morbidity: 12 children with polyarthritis, eight with carditis and five with Sydenham's chorea.
- Multiple medication needs are documented.
- Vigilance is important in the prevention of ARF.

Background

Acute rheumatic fever (ARF) 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 commonest 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 ARF 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 condition is sufficiently rare that 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

Demographic data

Of the 20 cases confirmed in 2005, there were nine in Ontario, six in Quebec and the remainder in Alberta and British Columbia. The average age at diagnosis was 10.1 years. The gender distribution was approximately equal, with 11 males and nine females.

TABLE 11

Acute rheumatic fever cases in 2005

Reported	Duplicates	Excluded	Under review	Confirmed
39	5	5	9	20

Systems affected

Eight patients had carditis meeting clinical criteria and six of them required ongoing medical therapy at the time of reporting. Therapy consisted of ACE inhibitors, digoxin and diuretics. None required surgical therapy at the time of reporting, although in one case mitral valve repair was planned. Twelve patients had polyarthritides meeting clinical criteria. Three patients had ongoing need

for anti-inflammatory medication at the time of reporting. Agents used were naproxen, ASA and indomethacin. Five patients had Sydenham's chorea; three reports included documentation of medical therapy. Agents used were valproic acid in two cases and haloperidol in one case. One patient had subcutaneous nodules and none were reported with erythema marginatum. No mortality was reported.

Long-term prophylaxis

All 20 children are receiving long-term prophylaxis against streptococcal infection. Three children are receiving monthly intramuscular injections of benzathine penicillin and the remaining 17 are receiving oral penicillin twice daily.

Conclusion

The second year of the ARF study has shown results consistent with the first year, with a very small number of confirmed cases nationally (20 cases in 2005 and 18 cases in 2004). These results confirm that acute rheumatic fever in children 18 years and younger is extremely rare. Within this small group, there is significant morbidity and the requirement for multiple medications, showing that there is a need for vigilance so that ARF is prevented whenever possible.

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Adverse drug reactions – serious and life-threatening

January 2004 to December 2007

Highlights

- Forty-four cases of suspected paediatric serious and life-threatening ADRs were confirmed.
- Antibiotics and anticonvulsants were the two drug classes most frequently suspected of causing ADRs.
- Participants documented patient outcome in 89% of ADR cases.
- Of reports received, 27% were complete.

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 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-saving treatment 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, as well as 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 18 years or less, associated with the use of prescription, non-prescription, biological (immunoglobulin) products, complementary medicines (including herbals), and radio-pharmaceutical products.

Exclusions

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

During 2005, there were 44 confirmed cases of suspected ADRs (Table 12). Seven reports were excluded for the following reasons: suspected cause of reaction – not a drug (n=3), self-administered overdose (n=2), incorrect diagnosis – not an ADR (n=1) and physician unable to recall case to complete the detailed report form (n=1).

TABLE 12

Suspected adverse drug reactions – serious and life-threatening cases in 2005

Reported	Duplicates	Excluded	Under review	Confirmed
71	1	7	19	44

Twenty cases concerned males, 17 concerned females, and in seven cases gender was not mentioned. The majority of cases (33/44) involved patients between six and 18 years of age. Twenty-seven (61%) of the children were Caucasian, two were Asian, two Italian, one Black and one of mixed race. In 11 cases no race was reported.

Drugs responsible for suspected adverse drug reactions

Table 13 lists all drugs suspected of causing ADRs. In 38 cases, one drug was suspected of causing the reaction. In six cases, two suspected drugs were involved.

TABLE 13

Suspected drugs (n=38) in ADR reports (n=44)

Suspected drug	# Reports
Amoxicillin	6
Carbamazepine, clarithromycin, ibuprofen, isotretinoin, methylphenidate, minocycline	2 each
Acetylcysteine, acetylsalicylic acid, allergen immunotherapy, arginine, atomoxetine, azathioprine, basiliximab, cefazolin, cefotaxime, cefprozil, ceftriaxone, ciprofloxacin, clindamycin, codeine, cyproterone acetate/ethinyl estradiol, goserelin, ifosfamide, infliximab, isoniazid, lamotrigine, palivizumab, peg-asparaginase, phenobarbital, phenylpropanolamine/chlorpheniramine/pseudoephedrine, pivampicillin, propofol, risperidone, somatropin, topiramate, trastuzumab, valproic acid	1 each

Patient outcomes resulting from suspected ADRs

Eighty-nine percent (89%) of the suspected ADR reports provided information about patient outcome (Table 14). Of note, more than one outcome was reported for most cases. At the time of reporting, 35 patients had recovered, three had not yet recovered, and one had died. The reported death, due to haemolytic crisis, followed the use of ceftriaxone. In five cases recovery status was not reported.

TABLE 14

Patient outcomes resulting from suspected ADR

Outcome	Frequency reported
Life-threatening reaction	11
Hospitalization	16
Hospitalization prolonged due to ADR	9
Disability	4
Required intervention to prevent damage/permanent impairment	15
Death	1
Emergency department visit	6
School absence	1
Unknown	5

Examples of suspected fatal or life-threatening reactions following drug administration as reported by participants or investigators are shown in Table 15.

TABLE 15

Suspected drugs reported with fatal or life-threatening ADRs

Suspected drug	Reported reaction(s)
Allergen immunotherapy	Hives, wheezing, difficulty breathing
Amoxicillin	Biphasic anaphylaxis
Arginine	Anaphylaxis
Azathioprine	Pancreatitis
Basiliximab	Respiratory insufficiency
Carbamazepine	Liver failure, atypical lymphocytosis, lymphadenopathy
Cefazolin	Anaphylaxis
Ceftriaxone	Hemolytic crisis
Goserelin	Recurrent anaphylaxis
Ibuprofen	Anaphylaxis, urticaria
Infliximab	Dyspnea, bronchospasm, diffuse rash
Isoniazid	Seizures, coma, acidosis
Isotretinoin	Pseudotumor cerebri
Palivizumab	Septicemia, meningitis (Strep B)
Peg-asparaginase	Shortness of breath, hypotension, vomiting
Topiramate/phenobarbital	Metabolic acidosis, decreased consciousness
Valproic acid	Thrombocytopenia, neutropenia

All but one suspected ADR were previously recognized reactions associated with the specific drug or drug class. One suspected ADR to somatropin may have resulted in the development

of pancreatic endocrine tumour and/or biliary tract obstruction. This reaction has not, to our knowledge, been previously reported.

Incomplete documentation occurred in nearly 75% of ADR reports. The most frequently missing data in reports were: drug dose, frequency of administration, concomitant drug therapy (if any), and dates of drug therapy and reaction. Therefore, causality assessment remains difficult. Participants assessed drug-ADR causality as definite (n=7), probable (n=32) and possible (n=7).

Conclusion

The two drug classes most frequently suspected of causing ADRs were antibiotics and anticonvulsants. Both drug classes are frequently used in paediatric care.

To adequately assess causality, it is critical that clinicians answer all questions: drug dose, frequency of administration, concomitant drug therapy and dates of drug therapy and reaction.

Further analysis of data collected through the CPSP since 2004 will be undertaken in the next

phase of this study. These analyses will determine the following: the level to which CPSP active surveillance captures information about serious and life-threatening ADRs not currently captured by existing spontaneous reporting systems; the usefulness of the data for meaningful analysis and interpretation of ADR risk; and the identification of health concerns regarding paediatric drug use.

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Congenital cytomegalovirus infection

March 2005 to February 2007

Highlights

- During the ten-month surveillance, 18 cases of congenital CMV infection were confirmed.
- Infants are often severely affected and diagnosed prenatally.
- First Nations children appear to be at increased risk of infection.
- Severely affected infants are treated with ganciclovir by Canadian paediatricians.

Background

Congenital cytomegalovirus (CMV) infection is the commonest 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, and 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 virus in the birth canal or breast milk. This infection has devastating consequences and is of great public health significance.

Although there has been significant international interest in congenital CMV, Canadian epidemiological data is minimal and at least 25 years old. Current data, specific to our own population, is essential for planning intervention practices. Active surveillance for congenital CMV infection is timely, as the following intervention strategies are on the horizon:

- The National Institutes of Health have recommended universal newborn hearing screening for early diagnosis and intervention to improve outcome in congenital deafness. However, this approach would miss much of the deafness caused by congenital CMV, which is progressive.

- Ganciclovir therapy in neonates with neurological manifestations of congenital CMV infection improves hearing outcome.
- CMV vaccines are currently being developed. Such vaccines would allow for primary prevention in CMV-susceptible women, analogous 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 with data 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

In the first 10 months of CMV surveillance, 18 cases were confirmed. Five reports were excluded as the diagnostic testing was not done early enough in life (within the first three weeks) to confirm the presence of congenital CMV infection, either because the diagnosis was not considered in the early neonatal period or the child was born and initially assessed in a remote centre without immediate access to diagnostic expertise or laboratory testing.

TABLE 16

**Congenital cytomegalovirus infection cases
March 1 to December 31, 2005**

Reported	Duplicates	Excluded	Under review	Confirmed
39	12	5	4	18

Demographics and epidemiological data

The majority of reported CMV cases were from Ontario (n=13) followed by Quebec (n=7) and Alberta (n=6). The remaining 13 cases were from five other provinces (NB, NL, BC, SK and MB). Three of the confirmed cases (17%) were from rural areas (population < 1,000) and all of these rural cases were born to First Nations women. Maternal ethnicity was as follows: Caucasian (33%), First Nations (28%), Asian (17%), Black and Latin American (6% each) and unknown (11%). Of the 18 confirmed cases, 14 of the mothers were born in Canada, one was born outside the country but had immigrated more than five years before and three were unknown. The mean age of the mothers is 24.4 years (range 17–41 years). Twelve (67%) of the mothers were primiparous.

Clinical Presentation

Five (28%) of the congenitally infected infants were diagnosed antenatally: one by serology and four by fetal imaging (three ultrasounds, one MRI). One of these infants was a stillbirth and the diagnosis, suspected by fetal imaging (showing intracranial calcifications, severe IUGR and hydrops) and maternal IgM, was confirmed by amniotic fluid PCR. The rest of the infants were diagnosed in the neonatal period and presented with symptoms ranging from low birth weight (with or without microcephaly) to thrombocytopenia,

hepatosplenomegaly, anemia and jaundice. All infants were diagnosed with a urine test positive for CMV and the majority by viral culture. Two were reported by PCR. One infant was diagnosed antenatally with amniotic fluid PCR (fetal urine). Newborn IgM serology was positive in only three of the infected infants; it was negative in five cases, not done in seven and unknown or missing in three.

Management

Most infants had cranial imaging with the following results: abnormal (n=8), normal (n=9) and not done (n=1). The results of the hearing assessment were as follows: abnormal (n=4), normal (n=11) and not done (n=3). The ophthalmologic assessment revealed the following: abnormal (n=3), normal (n=12) and not done (n=3). Of the reported infants, five received intravenous ganciclovir therapy. All of these infants had significant symptoms usually involving abnormal cranial imaging. Infected infants remained in the reporting hospital a total of more than 335 days. Paediatricians sometimes only reported the length of stay at their hospitals, 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 25.8 days (range 5–53 days). One infant was a stillbirth. No other infants died during the reporting period and all were discharged home or transferred to another facility.

Discussion

In the first 10 months, the surveillance study confirmed 18 cases of congenital CMV. The current rate of congenital CMV infection in Canada is not yet known. If the rate of congenital CMV infection 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 the following 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 to estimate the reporting rate through the CPSP for diagnosed cases); and neonatal symptoms may

be subtle and may not be 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.

Many of the cases (28%) were diagnosed prenatally by fetal ultrasound and these infants were relatively severely affected. Viral isolation or PCR testing confirmed the diagnosis. Neonatal IgM (as performed by the “TORCH” screen) had a low sensitivity. This emphasizes the possibility that infants diagnosed in the neonatal period may only represent the “tip of the iceberg”, and less severely affected infants may be missed for diagnostic purposes but still have significant neurological sequelae.

First Nations children appear to be at higher risk of congenital CMV infection. All infected children born in rural Canada were of First Nations origin.

Further data will be required to interpret these results. None of the mothers identified during this period were new immigrants to Canada. Observations about other risk factors, such as maternal occupation and household and daycare exposure, will have to await further data and analysis. Congenital CMV causes significant morbidity with affected infants experiencing prolonged hospital stays of high intensity.

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Congenital myotonic dystrophy

March 2005 to February 2008

Highlights

- Based on the four confirmed cases in the first year of the study, CMD is less common than anticipated.
- Most reported children have a mild phenotype with only one case requiring short-term ventilation.

Background

Myotonic dystrophy is an autosomal dominant multi-system disorder characterized by muscle weakness and myotonia commonly beginning in adulthood. There are two 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 effect of large accumulations of nuclear mutant mRNA. Similar to other trinucleotide repeat disorders, 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 symptoms in the newborn period (i.e., CMD), the parent who passes the gene defect is almost exclusively the mother. In fact, the mother 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.

CMD is diagnosed secondary to respiratory or feeding difficulties in the newborn period. However, signs during the pregnancy, including polyhydramnios and premature labour, may be the initial abnormality. No clear definition of CMD exists and prior studies may include individuals tested due to known family history and mild hypotonia not requiring any medical intervention. An incomplete correlation exists between the number of trinucleotide repeats and symptoms; individuals with larger repeat numbers generally show more severe symptoms. Rates of neonatal mortality and morbidity range widely. 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. Furthermore, the incidence of CMD has not yet been established through a population-based study and it is unclear how often children are the index case for their families or how families are using genetic counselling information.

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 have quality information on which to base 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 utilization 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 greater 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 four confirmed cases between March 1 and December 31, 2005. The 19 excluded cases were largely due to the diagnosis being made outside the surveillance period, although in four cases the diagnosis of CMD was not confirmed genetically and was not clearly myotonic dystrophy. All cases came from Central Canada.

TABLE 17

**Congenital myotonic dystrophy cases
March 1 to December 31, 2005**

Reported	Duplicates	Excluded	Under review	Confirmed
25	2	19	0	4

The four children for whom full information is available were all diagnosed in the newborn period and all had hypotonia and feeding difficulties. Only one required assisted ventilation for the first 11 days of life and a total hospital admission of 60 days. This child had a trinucleotide repeat expansion of 1,300. The other three children had feeding difficulties, which were the principal reason for admission to hospital longer than expected for their gestational age (range 1–3 weeks). One of these children required supplemental oxygen for the first 48 hours of life. The trinucleotide repeats in these three children were 700, 1,250 and 1,500.

Three of the children were the index case for their families. One mother had a known diagnosis, had mild symptoms, but had not received recent, specific prenatal counselling about the risk of transmission to a child and the phenomenon of genetic anticipation.

Although four confirmed cases is fewer than the 10 to 12 cases expected annually, efforts are being made to ascertain whether any cases have gone unreported through contact with molecular genetic laboratories and paediatric neurologists across the country.

A national cohort study has been set up that will follow consenting cases to evaluate the overall health and developmental consequences of CMD.

Conclusion

The CMD project identified four cases over the ten-month period; fewer than expected. As most of the cases reported came from Central Canada, there is a possibility of under-reporting. External validation methods will be used to determine if this is a legitimate concern.

Thus far, reported children have had a mild phenotype with feeding difficulties causing prolonged admission in the newborn period. Only one child needed ventilation, which was required for only 11 days. The number of trinucleotide repeats did not necessarily correlate with disease severity in this small sample. For example, the child with the longest repeat length (1,500) needed neither assisted ventilation nor nasogastric feeding.

Ongoing surveillance over the coming years will be important for drawing more firm conclusions from this study. CMD is an important disorder to study, 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 decisions.

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Early-onset eating disorders

March 2003 to February 2005 - Final report

Highlights

- During the two-year study, 160 cases were confirmed for a minimum incidence of 2.6 per 100,000.
- Children are seriously ill with an average weight loss of 7.4 kg (\pm 5) and almost half (48%) required hospitalization.
- Many cases did not meet the present DSM-IV diagnostic criteria for anorexia nervosa.
- For early detection of early-onset eating disorders, the use of growth charts is strongly recommended.

Background

Over the last 50 years, the prevalence of anorexia nervosa in young adolescents appears to have been increasing and it has been suggested that the age of onset of eating disorders appears to be decreasing. However, there is ongoing debate in the literature about how to apply the current diagnostic criteria for eating disorders to children and younger adolescents. What is known is that significant medical and psychological complications arise from starvation, weight loss or lack of appropriate weight gain during childhood and adolescence, making this group of conditions important to recognize and treat appropriately.

This study documents a minimum incidence of early-onset eating disorders (EOED) in Canadian children and provides descriptive data on the abnormal cognitions, behaviours and severity of weight loss or growth failure as a consequence. These otherwise unavailable data will aid in resource allocation and ultimately allow for better recognition of this condition in younger children, whose diagnoses may currently be missed or delayed.

Objectives

- 1) Describe the minimum estimated incidence of EOED in children and young adolescents aged five to 12 years in Canada.
- 2) Describe the range of medical and psychiatric clinical features at presentation.
- 3) Compare the clinical features in children and young adolescents with existing diagnostic criteria for eating disorders in older patients.
- 4) Describe current therapeutic interventions used in management.

Case definition

Any child from five to 12 years of age inclusively, seen in the previous month, with *newly* diagnosed EOED, where *eating disorder* is defined as:

- determined food avoidance
- and
- weight loss or failure to gain weight during a period of expected growth, not due to any identifiable organic cause such as celiac disease.

Exclusion criteria

Obese children in a supervised weight management program.

Results

Between March 2003 and February 2005, there were 160 confirmed cases of EOED. A summary of the results is presented in Table 18.

TABLE 18

Early-onset eating disorders cases
March 1, 2003 to February 28, 2005

Reported	Duplicates	Excluded	Under review	Confirmed
213	26	24	3	160

The incidence of new-onset eating disorders in children aged 12 and under was 2.6 per 100,000, with the incidence ranging from a low of 0.4 per 100,000 in males aged five to nine years to a high of 16.4 per 100,000 in females aged 12 years. The female to male ratio was 7:1 (137 females, 22 males and one unspecified) as compared to 10:1 in the older adolescent and adult population. The majority of children were Caucasian (91%), followed by Asian (4%) and the remainder included Latin American, Black,

Middle Eastern and mixed children. The majority of cases were from Ontario (39%), Quebec (34%) and British Columbia (10%). The other 16% of cases originated from Alberta, Manitoba and the Atlantic Provinces. No cases were reported from Saskatchewan or the Territories. The proportion of children with various clinical symptoms is summarized in Table 19.

TABLE 19	
Proportion of children with various symptoms	
Symptom	%
Food avoidance	98
Preoccupation with food	83
Weight loss	78
Fear of weight gain or fat	74
Preoccupation with weight	72
Denial of severity of symptoms	62
Perception that body is larger	57
Excessive exercise	51
Self-induced vomiting	11
Laxative or diuretic use	0
Bradycardia (<36 beats/min)	29
Hypothermia (<35.5°C)	13
Hypotension (BP<80)	21

The mean weight loss was 7.4 kg (\pm 5). The greatest weight loss was found in the group of children who were 12 years of age: girls in this age group lost an average of 8.9 kg (range 1–28 kg), approximating 23% of their total body weight; boys in this age group lost an average of 8 kg (range 2–15 kg), approximating 21% of their total body weight. Ninety-two percent (92%) of cases of EOED were identified in children over the age of nine. In that group, 100% (n=20) of males but only 77% (99/128) of females had lost weight. Averaged out over all confirmed cases, only one male had not lost weight (5%) compared to 26 females (19%). Fourteen of the 26 females who had reached menarche had secondary amenorrhea.

The majority of children did not have a history of a co-morbid psychiatric diagnosis but 28% had anxiety and 16% depression. A positive psychiatric family history was reported in 36% of cases and 49% had changes in their social situation. Almost half (48%) required an inpatient admission for treatment.

A latent class analysis was performed on the eating symptoms listed above that separated the population into two distinct groups. The first group comprised 64% of the total population and exhibited symptoms consistent with anorexia nervosa. The second group fell into the category of eating disorder not otherwise specified (EDNOS). This appears to be a distinct group and may represent food-avoidant emotional disorder (FAED) as described by the Great Ormond Street criteria (an alternative classification for the range of eating disorders of childhood proposed by Bryant-Waugh and Lask).

TABLE 20			
Diagnostic clusters			
	Anorexia nervosa (n=103)	Food-avoidant emotional disorder (n=57)	Statistical value
Mean age	11.1 years	10.3 years	p=0.003
Food avoidance	99%	95%	ns*
Weight preoccupation	88%	42%	p<0.001
Fear of weight gain	93%	39%	p<0.001
Denial of symptoms	71%	47%	p<0.05
Over-exercising	76%	5%	p<0.001
Somatic complaints	15%	63%	p<0.001
Self-induced vomiting	14%	7%	ns*
Average weight loss	8.4 kg \pm 5.4	5.2 kg \pm 3.3	p<0.001
Admitted to hospital	54%	36%	p<0.05

* Not significant

Conclusion

Paediatricians and psychiatrists are identifying children and younger adolescents with eating disorders. The majority of identified children present with important weight loss and are seriously ill. Food avoidance was the predominant clinical feature in all confirmed cases. Many children also displayed a preoccupation with food and weight and a fear of gaining weight. However, like older adolescents, over half of these children denied their symptoms. Some children endorsed the symptom of vomiting (11%). This finding has traditionally been thought to occur in older adolescents and therefore requires further investigation.

One important feature documented in this study is that some children did not lose weight (one male, 26 females). However, failure to gain weight during important growing years is a significant phenomenon that is not presently captured by the DSM-IV criteria. These data reinforce the importance of using growth charts where a fall off the curve would be more evident and would facilitate earlier detection of all cases, especially males.

Finally, one of the criteria for diagnosing anorexia nervosa in females is amenorrhea. Children less than 12 years old would not necessarily be at an age where menarche would have occurred and therefore the criterion of amenorrhea (loss of three consecutive menstrual periods) may not be useful for the diagnosis of anorexia nervosa in children and younger adolescents. In this study, 14 out of 26 females met the criteria for secondary amenorrhea. Consequently, almost half of the children did not meet the full criteria for anorexia nervosa as outlined in the DSM-IV. This suggests that it may be difficult to apply the current DSM-IV criteria to children and younger adolescents. There may also be problems in matching clinical populations to the existing classification systems that are based on adults with eating disorders. Developmentally, children have limited ability for insight that would be required to endorse the full spectrum of symptoms.

Furthermore, children and younger adolescents may present with types of clinical eating disturbances that are different from the classic eating disorders of anorexia nervosa and bulimia nervosa with respect to core psychopathology.

Nonetheless, the presenting symptoms are as medically and psychologically problematic. A full 30% of this population presented with significant weight loss (mean 5.2 kg), food avoidance and somatic complaints, but did not endorse other hallmark symptoms of fear of gaining weight, weight or shape preoccupation, over-exercising, purging or denial of severity of symptoms. Thirty-five percent (35%) of this group were severely ill and required hospitalization. It may be that these children are presenting in ways that will require a redesign of the diagnostic categories, taking into consideration the entity of FAED as described by the Great Ormond Street criteria.

This study is based on a similar data collection undertaken by the Australian Paediatric Surveillance Unit. So far, the profile of clinical features for identified cases at the time of diagnosis is consistent with those being reported in Canada. International comparisons of the data from the EOED studies will enhance our knowledge of this global problem and will contribute to our understanding of EOED throughout the world.

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

March 2005 to February 2007

Highlights

- During nine months of surveillance, 43 cases of head injury secondary to suspected child maltreatment were confirmed.
- Injuries resulted in moderate to severe neurological sequelae in 35% of cases or in death in 18%.
- Child welfare authorities had previously been involved in 34% of 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 followed to protect these 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 and differ considerably from actual case studies reported through the legal and/or medical systems. These differences can be attributed to factors such as 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 (SBS) and the other was limited to cases where the 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 data collection 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 has 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 evidence 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 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 43 cases confirmed to date, 35% were from the Western provinces (British Columbia, Alberta and Manitoba), 47% were from Central Canada (Ontario and Quebec) and 19% were from Eastern Canada (New Brunswick and Nova Scotia). The median age at initial presentation was 4.5 months (n=38, range 1–42 months). There were 30 boys and 13 girls. Of those cases where numbers of children in the household were reported (91%), the median number of children was two (range 0–5).

TABLE 21

Head injury secondary to suspected child maltreatment cases, March 1 to December 31, 2005

Reported	Duplicates	Excluded	Under review	Confirmed
105	25	6	31	43

Management

Of the confirmed cases, 84% 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 0–131). The initial presentation included decreased consciousness (49%), lethargy (42%), seizure (33%), vomiting (28%), irritability (21%), apnea (21%), respiratory difficulty (14%) and soft tissue injury (14%). All but three of the 43 confirmed cases were hospitalized. Data on length of stay were available for 29/43 cases, with a median length of stay of 11 days (range 1–61 days). Two-thirds of the cases were admitted to the intensive care unit (ICU). Data on length of ICU stay were available for 15/28 cases, with a median length of stay of three days (range 1–9 days). All but two of the cases involved a hospital child protection team and the police. Of the 41/43 confirmed cases with available information, child welfare authorities had previously investigated in 14/41 cases (34%).

Injuries

All cases had at least one clinical finding that included subdural hematoma (88%), retinal hemorrhage (58%), fractures of long bones or ribs (44%), bruising (44%), seizures (42%), cerebral edema (35%) and skull fractures (23%). Previous medical history was reported for 18 of the cases and the most frequent issues were excessive crying, feeding difficulty, prematurity and colic. SBS was the suspected diagnosis in 74% of the cases and 44% had a diagnosis of other physical abuse suspected. Medical status at time of discharge was available for 40 cases. In seven of these cases (18%) the injuries resulted in death and in 14 cases (35%) there was moderate to severe neurological sequelae.

Perpetrator

Perpetrator status was confirmed in 12% of cases, suspected in 60% and unknown in 28%. In 20/32 cases, the perpetrator was a male and in 24/32, the perpetrator lived with the child. The relationship of the perpetrator to the child and a history of risk factors were available for 33/43 cases. The perpetrator was a parent in 64% of these cases, followed by mother's partner (18%). Almost half (16/33) 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

The first nine months of this study have shown that head injury secondary to suspected child maltreatment (abuse or neglect) in children up to 14 years of age is prevalent in our society with 43 cases confirmed at a median age of 4.5 months, and almost three-quarters of those diagnosed as suspected SBS. There was significant mortality and morbidity among the confirmed cases. In the 40 cases where the outcome was known at the time of discharge, 18% resulted in death and 35% had moderate to severe neurological sequelae.

With over 80% of reported cases presenting to an emergency department, there is a need for adequate clinical preparation of health care providers in the identification of these cases. The fact that child welfare authorities had previously been involved in 34% (14/41) of the cases with available information reinforces the importance

of support and close follow-up of the families. It is hoped that this study will provide data that can inform efforts to improve recognition of these cases by health care professionals and lead to more effective prevention efforts.

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Lap-belt syndrome

September 2003 to August 2005 - Final report

Highlights

- The study confirmed 28 cases of lap-belt syndrome with high prevalence of spinal fracture (43%) and permanent spinal cord lesion (25%).
- Although 12 children were less than eight years old, only one was restrained in a booster seat (wearing only a lap belt).
- Seat belts save lives; however, if worn incorrectly they can cause important abdominal and lumbar spine injuries.
- There is an urgent need for aggressive education efforts to ensure adequate child restraint use in motor vehicles.

Background

Motor vehicle crashes represent the leading cause of death and disability in children. The use of seat belts has clearly reduced fatalities and severity of injuries in motor vehicle crashes. This has led organizations such as the Canadian Paediatric Society and Transport Canada to provide guidelines for age-appropriate restraint. With the increasing use of seat belts over the last decades, a new association of injuries has emerged among adults and children involved in motor vehicle crashes. 'Seat-belt syndrome' was first described by Garrett and Braunstein in 1962 and refers to injuries to the intestinal viscera and to the lumbar spine associated with seat-belt restraints. Children are especially vulnerable to these injuries as their intra-abdominal organs are less protected by the thorax and pelvis, they have a lower centre of gravity and their iliac crests are less developed than those of adults, allowing the belt to ride up over the abdomen. To date, there have been very few paediatric studies on the incidence of seat-belt syndrome.

Objectives

- 1) Obtain epidemiologic data on the incidence and pattern of injuries encountered in the lap-belt syndrome.
- 2) Identify at-risk age groups.
- 3) Supply data that will help develop new strategies to adequately protect children in motor vehicles.
- 4) Promote education and awareness of this rare syndrome among health care professionals.

Case definition

Any child up to and including 18 years of age restrained in a motor vehicle at the time of a crash,

with either an abdominal injury, as determined by operation or CT scan, or thoraco-lumbar spine injuries with or without spinal cord injuries.

Results

Twenty-eight children with injuries compatible with lap-belt syndrome were confirmed.

TABLE 22

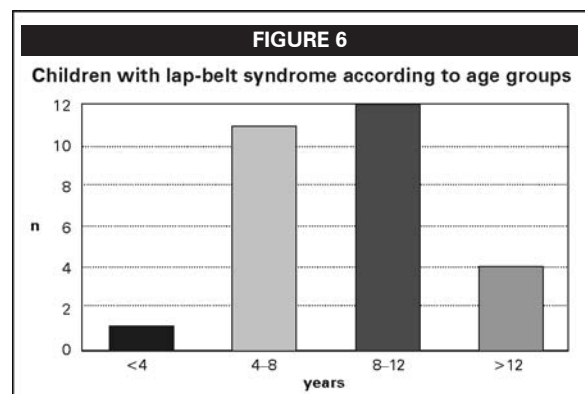
Lap-belt syndrome cases
September 1, 2003 to August 31, 2005

Reported	Duplicates	Excluded	Under review	Confirmed
41	3	7	3	28

Their ages ranged between two and 15 years with a median of eight (Figure 6). Fourteen were girls. The average Pediatric Trauma Score was seven (range 3–10). In six crashes, there was a death of another passenger in the car. Most of the crashes were head-on collisions (17/28). The median speed at the time of impact was 97.5 km/h (range 50–120 km/h). Most of the children (23/28) were seated in the back of a passenger car or a mini-van. Three children were seated in the middle front seat of a pick-up truck and two were front-seat passengers. Although 12 children were less than eight years old, only one was restrained in a booster seat (wearing only a lap belt). Only three of the older children were properly restrained with a three-point seat belt.

Twenty-seven children were hospitalized. The median hospital stay was 10 days (range 3–155 days) excluding rehabilitation. Eighteen children were admitted to a paediatric intensive care unit (ICU) and the median ICU stay was five days (range 1–21 days). All of the children survived

their injuries. Twenty-three underwent at least one surgical intervention and 10 had two or more interventions.



Twenty-four children had an abdominal lesion. Of these, 17 had an intestinal injury (13 small bowel perforations, three small bowel infarcts, one delayed small bowel stricture, four colon perforations and two sigmoid lacerations), eight had mesenteric tears, three had hepatic lesions, one had a biliary tract laceration, five had splenic lacerations and three had a renal contusion. Fourteen patients had an abdominal wall ecchymosis or contusion associated with abdominal injury.

Twelve patients (43%) had lumbar spine fractures (five Chance-type fractures, four compression fractures of a vertebra, two fracture-dislocations of L2–L3 and one comminuted fracture of L2). Seven of these patients (7/28, 25%) presented with a complete paraplegia below the level of the lesion and none recovered.

With regard to other injuries, no patient had a major head trauma and six patients had thoracic injuries ranging from pulmonary contusion and hemothorax (n=4) to ruptured diaphragm (n=2). Bone fractures other than spinal fractures included pelvis (n=2), sacrum (n=1) and long bone (n=4).

Discussion

At least 28 children in Canada suffered from lap-belt syndrome over a 24-month period. All age groups were represented; however, 79% of the children were between four and 12 years of age. In congruence with a recently published study (Durbin DR et al. *Pediatrics* 2005;115(3):e305-9), the results of this study show that age-appropriate

restraint use is a major protective factor in motor vehicle crashes. It is very worrisome that only four out of 28 children (14%) reported in this study were adequately restrained according to their age (use of booster seat under eight years of age and a three-point seat belt for the older children). Furthermore, children between four and 12 years old seem especially at risk for lap-belt syndrome. These children have outgrown their child safety seats and are often restrained in seat belts designed for adults, which should not be considered an acceptable alternative to booster seats for children under the age of eight. The children described in this study presented with a large spectrum of abdominal injuries, including the classically described intestinal lacerations and mesenteric tears, but also solid organ lacerations and ruptures. The spectrum of abdominal injuries noted in children with lap-belt syndrome seems wider than the classically described hollow viscous injuries in adults. The high prevalence of spinal fracture (43%) and permanent spinal cord lesion (25%) is a catastrophe.

Conclusion

These study results call for high vigilance among physicians for lap-belt associated injuries in restrained paediatric victims especially if they present with ecchymosis, contusions or abrasions over the abdomen. Restrained children in motor vehicle crashes present with a wide spectrum of injuries; they have more abdominal solid organ injuries, a wider spectrum of spinal cord injuries than adult patients, and a high incidence of complete paraplegia. These results also emphasize the need to review restraints in motor vehicles to protect children adequately and the urgent need for aggressive education efforts and law enforcement aimed at ensuring adequate child restraint use in motor vehicles.

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Medium-chain acyl-coenzyme A dehydrogenase deficiency

September 2005 to August 2007

Highlights

- The exact incidence of MCAD deficiency in Canada is still largely unknown.
- One patient with MCAD deficiency has been confirmed since the initiation of the study.
- Newborn genetic screening is ongoing in four provinces (BC, NS, PE and SK) and will start in Ontario in 2006.

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 deficiency is one of the enzymes involved in the fatty acid beta-oxidation pathway. The commonest presentation is during infancy when a relatively well child may decompensate 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. There is an extremely high risk of mortality of up to 25% at the time of the initial presentation. Another clinical presentation is unexplained infant death (SIDS). Interestingly, some individuals with this disorder can remain asymptomatic, thus leading to great variability in the clinical phenotype.

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

Treatment of this condition is fairly straightforward and involves avoidance of fasting and ensuring

adequate glucose intake during illnesses. Parents are provided with a protocol for management during acute sicknesses. A carnitine dose of 100 mg/kg three times per day is given in childhood; however, there are still controversies as to its benefit with prolonged use.

The exact incidence of MCAD deficiency in Canada is still largely unknown due to lack of universal newborn screening. With the advent of genetic screening and the use of tandem mass spectrometry, neonatal screening for this disorder is now occurring in a number of countries, including some American states and four Canadian provinces (BC, SK, PE and NS); newborn screening will start in Ontario in 2006. MCAD deficiency has an excellent prognosis when treated early and has significant genetic implications for future pregnancies and other family members, thus making a strong case for newborn screening.

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, 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–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
- 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

During the first three months of the surveillance study, there was one confirmed case of MCAD deficiency. This case was detected in a province with a newborn screening program. The infant was asymptomatic. The diagnosis was confirmed by the presence of A985G mutation in homozygous form. The diagnosis very early in life allows for the implementation of measures during acute illnesses to prevent starving and offers an excellent prognosis.

TABLE 23

Medium-chain acyl-coenzyme A dehydrogenase deficiency cases in 2005

Reported	Duplicates	Excluded	Under review	Confirmed
2	0	1	0	1

Conclusion

Active surveillance of MCAD deficiency is timely, as it will allow for comparison between provinces with and without universal newborn screening. Since 25% of patients with MCAD deficiency die at their first presentation, Canadian pathologists, particularly coroners, have been recruited to participate in this study in the hope of improving case ascertainment. This study will provide data on incidence, burden of illness and clinical outcome, which might guide public health policy in terms of advocating for universal newborn screening for MCAD deficiency.

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Osteogenesis imperfecta

January 2004 to December 2005 - Final report

Highlights

- Twenty-seven cases of OI were confirmed in various ethnic groups, with eight additional cases presently under review.
- Eleven cases sustained five or more fractures at the time of diagnosis.
- Three patients were evaluated for physical abuse prior to being diagnosed with OI type I.
- Thirteen of the 27 cases are presently receiving treatment with a bisphosphonate agent.

Background

Clinical spectrum of osteogenesis imperfecta

Osteogenesis imperfecta (OI) is a heritable form of osteoporosis, which usually presents in childhood. Four different types of OI are commonly distinguished on the basis of clinical features and disease severity, according to the classification proposed by Sillence. Patients with OI type I have a mild phenotype with normal or near-normal height and typically blue sclera, while OI type II is usually lethal in the perinatal period. OI type III, known as progressive deforming OI, is the most severe form in children surviving the neonatal period. These patients have a characteristic phenotype including the following: extreme short stature; severe deformity of the spine, thoracic cage and extremities; white or blue sclera; and often triangular facies. Patients with a moderate to severe form of the disease who do not fit one of the above descriptions are classified with OI type IV; as such, this group is extremely heterogeneous. According to Sillence and Lubs, patients with the type I phenotype represent 60% of patients with OI, followed by OI type III (20%), type II (10%) and type IV (< 10%).

In the majority of cases, OI is inherited as an autosomal dominant trait, though autosomal recessive transmission and gonadal mosaicism have also been described. In about 85% of OI patients, mutations in the genes encoding type I collagen, COL1A1 and COL1A2, can be found. Thus, although collagen type I mutations are frequent in OI, the lack of a detectable mutation does not rule out the diagnosis.

The Sillence classification for OI has recently been expanded, by characterizing three additional phenotypes with distinct clinical and histological features (named OI types V, VI and VII).

Patients with OI type V demonstrate a striking radiological triad of hypertrophic callus formation, interosseous calcification of the forearm, and a dense metaphyseal band under the growth plate. The inheritance suggests autosomal dominant transmission. Patients with the OI type VI phenotype show subtle distinguishing clinical features such as normal sclera and teeth. There is a moderate elevation in alkaline phosphatase levels, as well as characteristic histological features that include increased osteoid thickness and disordered bone lamellation. Despite the mineralization defect at the bone tissue level, there is no evidence of a disorder of mineral metabolism, and mineralization of the growth plate is unaffected. The mode of inheritance in OI type VI is unknown. OI type VII follows autosomal recessive inheritance, recently described in a consanguineous First Nations community from Northern Quebec. Rhizomelia and coxa vara are striking characteristics of the disease, associated with slightly blue sclera, normal dentition and moderately severe long bone deformity. This form of OI has been linked to chromosome 3p, outside the type I collagen loci. The precise genetic defect in OI type VII remains to be elucidated.

Changing face of OI: bisphosphonate therapy

Frequent fractures and the resulting pain and immobilization are major causes of morbidity among patients with OI. In recent years, the quality of life of children with severe OI has improved remarkably through the administration of cyclical intravenous pamidronate, in conjunction with multidisciplinary (surgical and rehabilitative) care. Now that effective treatment is available, prompt diagnosis and initiation of medical and supportive therapy during early life are paramount to enhancing the quality of life of patients with OI. In addition to intravenous pamidronate, studies of other bisphosphonates, including oral agents,

are ongoing with the aim to ultimately provide clinicians with a variety of treatment options for patients with OI of differing severities.

Need for current incidence data

The most reliable estimates of the frequency of OI to date are based upon reports of fractures occurring in the newborn period. However, neonatal fractures are unlikely in OI type I, and may or may not occur in OI types III to VII. While the incidence of the disease is estimated to be 1:20,000 to 1:60,000 live births, the true incidence of OI is likely to be much higher. These estimates were established more than 15 years ago, before newer diagnostic techniques (collagen mutation analysis, bone densitometry) became widely available.

Objectives

Primary

Determine the incidence of OI in Canada by ascertaining all newly diagnosed cases over a two-year period.

Secondary

- 1) Raise physician awareness in Canada regarding OI in general, and the novel forms in particular, so that diagnoses of OI can be made in a timely fashion and appropriate treatment can be initiated during the critical years of bone growth and development.
- 2) Identify patients and/or kindred with novel OI forms (OI types V to VII), for whom the genetic basis is presently unknown, to obtain clinical and genetic information, which may ultimately lead to mutation identification.
- 3) Determine whether a geographic distribution of OI exists, so that regions in need of a local OI intervention program (including medical, orthopaedic and rehabilitative care) can be identified.
- 4) Educate medical health providers and child welfare workers regarding the heterogeneous manifestations of OI, with the aim of facilitating the differentiation of the abused child from the child with congenital bone fragility due to OI. This, in turn, may prevent or minimize false allegations of child abuse.

Case definition

Report any child up to and including 18 years of age with:

- a new diagnosis of OI, defined as a congenital bone fragility condition associated with low bone mass, diagnosed during the study period; and
- clinical features in keeping with a diagnosis of OI types I to VII (see Table 1 of the protocol).

Exclusion criteria

- Bone fragility due to other causes, including genetic disorders (e.g., Ehlers Danlos syndrome), iatrogens (steroids, methotrexate, coumadin, radiotherapy), neuromuscular disease, chronic illness, endocrinopathies and idiopathic juvenile osteoporosis
- Fractures due to child abuse

Results

Between January 2004 and December 2005, there were 27 confirmed cases of newly identified OI reported through the surveillance program. Fourteen of the confirmed cases were girls.

TABLE 24

**Osteogenesis imperfecta cases
January 1, 2004 to December 31, 2005**

Reported	Duplicates	Excluded	Under review	Confirmed
70	20	15	8	27

Demographic profile and OI phenotype

The majority of confirmed cases were from Ontario (63%) and British Columbia (26%). Three other provinces accounted for the remainder (AB, NL and QC). The distribution of confirmed cases by phenotype (Table 25) was as follows: 16 OI type I (59%, seven girls), two OI type II (7%, one of each gender), four OI type III (15%, four girls) and four OI type IV (15%, two girls). The type of OI was not indicated in one case; however, the clinical description was highly suggestive of OI type III or IV. There were no cases of OI type V, VI or VII identified. The mean age at diagnosis for all sub-groups combined was 4.8 years (SD 5.6, range 0.4–17). Ten patients were diagnosed in the first month of life, with two of these patients having been diagnosed antenatally. Pregnancy was terminated in one of the two antenatally diagnosed cases. The majority of the cases were Caucasian (67%, n=18), two were Asian and one was Indian. Six patients were of combined ethnicity (two were First Nations/Caucasian and there was one of each of the following: Asian/Caucasian, Black/Caucasian, Middle Eastern/Caucasian and unknown/Caucasian).

Clinical presentation

The mean age at time of first fracture was 13.5 months (SD 16.4, range 5.25–60). Twenty-two percent (22%, n=6) of cases had sustained five to 10 fractures by the time of diagnosis, five cases had sustained more than 10 fractures and 13 reported fewer than five fractures. One case did not have any prior history of fractures and the number of fractures was unknown in two cases. The number of fractures at time of reporting per OI sub-type is presented in Table 26. Three of the cases, all with OI type I, had been evaluated for an allegation of physical abuse before the diagnosis of OI was made. Of these cases, blue sclera were present in all three and there was a family history of OI in one case. Thirteen of the 27 cases had a known family history of OI, 11 did not, and the information was unavailable in three cases. Eight cases had undergone type I collagen studies as part of their evaluation.

Therapeutic intervention

Thirteen of the 27 confirmed cases were receiving bisphosphonate therapy at the time of reporting, 10 were not being treated medically and the information was unknown in three cases. In one additional case, pregnancy was terminated. Eleven of the 13 treated patients were prescribed intravenous pamidronate; the type of bisphosphonate was not specified for two patients. One of the 13 treated cases was participating in an institutional review board approved protocol at the time of reporting. The other treated patients were offered therapy outside of research studies. Seven of the 13 treated cases had OI type I and the other six treated patients had OI type II, III or IV. Nine of the 10 patients who were not being treated medically at the time of reporting had the mild (OI type I) phenotype. One untreated patient had the moderate (OI type IV) phenotype.

Conclusion

Over the two years of this surveillance study, 27 OI cases from various ethnic groups were confirmed in Alberta, British Columbia, Newfoundland and Labrador, Ontario and Quebec. The majority of cases (59%) manifested the mild OI phenotype (type I), followed by OI types III, IV and II. The distribution of the OI sub-types was similar to reports in the literature. There were no reports of the more recently described OI phenotypes (type V, VI or VII). Three cases of OI type I were evaluated for possible physical abuse before being diagnosed with congenital bone fragility, including one case in which there was a family history of OI. In all cases

of initially suspected abuse, blue sclera, one of the classical clinical stigmata of OI, was present. These results highlight the importance of raising physician awareness of the association between sclera hue and congenital bone fragility, to avoid misdiagnosis of physical abuse in the OI setting. Almost half of the cases, the majority of which had OI type I, were offered bisphosphonate therapy, most often in the form of intravenous pamidronate. Prompt diagnosis and initiation of medical and supportive therapy during early life are paramount to enhancing the quality of life of patients with OI. This will also optimize conservative measures to enhance bone health and prevent symptomatic osteoporosis.

TABLE 25

OI cases distribution by phenotypes

OI phenotype	Numbers of cases (Total = 27)
Type I	16 (7 girls)
Type II	2 (1 girl)
Type III	4 (4 girls)
Type IV	4 (2 girls)
Unknown	1 (male)
Types V, VI, VII	0

TABLE 26

Mean age at the time of reporting and number of lifetime fractures, per OI phenotype

	Type I n=16	Type II n=2	Type III n=4	Type IV n=4	Unknown n=1
Mean age at time of reporting in years (SD)	6.6 (5.3)	-0.2 (0.3)	-0.1 (0.2)	5.8 (7.7)	0.75
Number of lifetime fractures	Number of patients				
0 fractures	1	0	0	0	0
<5 fractures	9	0	2	2	0
5 to 10 fractures	4	0	1	1	0
>10 fractures	2	1	1	1	0
Unknown	0	1	0	0	1

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Severe combined immunodeficiency

April 2004 to March 2007

Highlights

- Seven cases of SCID were confirmed.
- Six of the confirmed cases were referred for bone marrow transplant.
- None of the cases thus far were reported in Aboriginal children.

Background

Severe combined immunodeficiency (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 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 of the children 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, greatly exceeding 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 is required to make an evidence-based decision 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 BCG vaccination.

SCID, a group of rare genetic disorders characterized by profound abnormalities in T and B and natural killer cell development and function, was first reported more than 50 years ago. In the past two decades, great advances have been made in the understanding and

treatment of SCID. 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 recombinae 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 due to an ADA deficiency (about 15–20%).

General estimates of the incidence of SCID are 1 in 75,000–100,000 live births, with higher than expected rates in Switzerland at 24.3 in 100,000 live births and in the United States Navajo population at 52 in 100,000 live births. No Canadian incidence data for SCID is available.

Objectives

- 1) Estimate the incidence of SCID in Canada.
- 2) Estimate the incidence of SCID in Aboriginal children in Canada.
- 3) 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 $3,000/\text{mm}^3$ 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 seven confirmed cases of SCID in 2005. Six are males and one is female. All but one of the children were born in Canada. The average age at diagnosis was 10.6 months (range 4–17 months). Confirmed cases include: two cases of ADA deficiency, one case of major histocompatibility complex class II (MHC II), and one case of zeta-chain-associated protein kinase 70 (ZAP 70). The type of SCID has not been determined in the other three confirmed cases.

TABLE 27

Severe combined immunodeficiency cases in 2005

Reported	Duplicates	Excluded	Under review	Confirmed
19	8	1	3	7

The main clinical features include interstitial pneumonia (86%), persistent bronchiolitic-like illness (71%) and opportunistic infections (71%). Four of the seven cases showed failure to thrive and four cases also showed other significant infections (e.g., CMV, HSV1, severe impetigo, pneumonia and sepsis).

Six of the confirmed cases were referred for bone marrow transplant (BMT), but only one had received it by the time of reporting. Three patients were awaiting either a decision on BMT or waiting for the procedure. One patient was referred but was determined not to be a candidate for BMT. One of the patients had died and four remained in the hospital when the reports were received.

Based on the 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. Data received to date indicate that 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. No cases have been found in Aboriginal children. This study has been extended until March 2007 and may continue beyond that point if warranted.

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Transfusion-related acute lung injury

September 2005 to August 2007

Highlights

- TRALI has recently become the most common cause of transfusion-related death.
- The incidence in the paediatric population is unknown.

Background

Transfusion-related acute lung injury (TRALI) is a rare but severe reaction, which can be fatal. Patients develop acute lung injury rapidly, within six hours of initiating a transfusion of any blood product containing plasma (red blood cell, platelets, 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 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 in the paediatric population is unknown; incidence in the adult population varies from 1:1,000 to 1:560,000, depending on the blood product involved. The reaction is due to the presence of antibodies and/or biologically active lipids in the plasma of donors, which react with the recipient's antigens and/or activate already primed recipient's neutrophils. Patients with predisposing factors are more at risk to develop this complication (see case definition).

Objectives

- 1) Determine the incidence of TRALI using a standardized definition.
- 2) Describe the characteristics of patients and the associated clinical signs and symptoms of this transfusion reaction.
- 3) Describe the treatment and outcome.
- 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 Toronto in April 2004 (Kleinman S, Caulfield T, Chan P, et al. Toward an understanding of transfusion-related acute lung injury: statement of a consensus panel. *Transfusion* 2004; 44(12):1774-89).

Results/discussion

As TRALI is a very rare phenomenon, it is not surprising that no cases were reported to the CPSP in the first four months of surveillance. TRALI is recently becoming the most common cause of transfusion-related death. However, since this complication presents as a clinical syndrome without a pathognomic confirmatory laboratory test, under-diagnosis and under-reporting are highly suspected. It is important to recognize TRALI in order to immediately alert the blood bank to prevent administration of same donor blood to other patients, thereby avoiding further TRALI episodes.

Conclusion

This CPSP study is the first one to assess national incidence, presentation and burden of illness

in the paediatric population. Further effort to raise awareness of this serious life-threatening complication is needed.

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New studies in 2006



Kernicterus

September 2006 to August 2008

“Understanding the risk factors of kernicterus and its re-emergence in Canada will contribute to preventing neurological complications in newborns.”

Severe neonatal hyperbilirubinemia continues to be a major problem in Canada in otherwise well term and near-term infants, despite the ability to identify jaundiced newborns at discharge. Sequelae of severe hyperbilirubinemia include bilirubin-induced neurologic dysfunction (BIND) and kernicterus. The re-emergence of kernicterus in the last 10 to 15 years is particularly worrisome since it is a largely preventable disease. Although kernicterus was originally used as a pathological term, it is now used commonly by paediatricians to describe permanent neurological damage in children affected by severe jaundice. The clinical characteristics of kernicterus and BIND can change over time and include abnormalities in tone, movement disorders, sensori-neural hearing loss, gaze abnormalities, dental problems, as well as consistent MRI findings.

The incidence and prevalence of kernicterus in Canada is currently unknown. Case series have been reported in the last two years. Kernicterus monitoring is currently underway in the United States and some European nations but, to

date, there has been no systematic nationwide surveillance.

This study will gather Canadian data on identifying cases of kernicterus and BIND. The CPSP is ideal for understanding rare events and will be used to estimate the prevalence of kernicterus or BIND in Canada as well as identify epidemiological and medical risk factors in order to prevent neurological swelling from hyperbilirubinemia. The study results will assist in ensuring the appropriate interventions for jaundiced newborns at the time of discharge to prevent neurological complications.

Principal investigator

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Non-type 1 diabetes mellitus

April 2006 to March 2007

“The landscape of diabetes in Canadian children is changing and needs to be better documented.”

Diabetes mellitus 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 including type 2 diabetes mellitus (T2DM), monogenic forms of diabetes and secondary diabetes, including medication-induced diabetes mellitus (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 medication-induced diabetes may be mediated, directly or indirectly, by increased body weight; both can be difficult to distinguish from T2DM.

Type 2 diabetes mellitus is considered a major public health problem. The disease burden is considerable with some studies demonstrating development of diabetes-related micro-vascular and macro-vascular complications in young adulthood. The economic consequence of T2DM and its related complications in Canadian children could be substantial. In 1997, the total direct cost of obesity in Canada was greater than \$1.8 billion and health care costs attributable to T2DM were the second largest, at \$423.2 million. The development of diabetes-related complications in young adults may have a drastic impact on the need for limited health resources in Canada.

Data on the incidence and prevalence of non-type 1 diabetes mellitus (NT1DM) in Canadian children are limited. Currently, a global effort is underway to conduct population-based epidemiological studies to quantify the problem.

It is imperative that Canadian data be obtained because of Canada's unique ethnic, cultural, geographic and behavioural characteristics. There is a need to gain a better understanding of the magnitude, characteristics and public health consequences of this disease.

This study will provide epidemiological and demographic data about Canadian children with NT1DM and specifically obesity-related T2DM. It will provide a foundation upon which health promotion and disease prevention programs can be established.

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Survey Questions

Adolescent depression and side effects of selective serotonin reuptake inhibitors

November 2005

According to the World Health Organization, depression will be the leading cause of disability worldwide by the year 2020. Commonly, depressive disorders begin in adolescence and up to 60% of adolescents with depression will have a recurrent episode as an adult. Given the high burden of suffering with depressive disorders in this population and the high risk of recurrence, efficacious and safe treatments are clearly needed. However, there has been recent controversy about the use of non-tricyclic antidepressants, one form of treatment previously thought to be efficacious and safe in this age group.

After reviews of the efficacy and safety of non-tricyclic antidepressants in youth with depression, both the American Food and Drug Administration (FDA) and Health Canada have released warnings about the use of any of these agents in youth with depression. In particular, the FDA released its strongest caution – a “black box” warning – regarding the use of these medications in patients with depression.

The purpose of this survey was to ascertain the impact of the “black box” warning on the use of antidepressants by Canadian paediatricians. Other information gathered in this survey included the practice patterns of paediatricians in Canada regarding the diagnosis of depression and treatment with antidepressants.

Responses were received from 544 (23%) of the 2,395 participants. Seventy-five percent (75%, n=408) of the respondents diagnosed and/or managed adolescents with depression in their practices. Of these, 59 (14%) of the respondents were not aware of the “black box” warning.

Of the 349 respondents who were aware of the warning, 85% (n=296) changed their prescribing

practices. Thirty-one percent (31%, n=108) followed their patients more closely, while 26% (n=90) referred them to psychiatry. Twenty-nine (8%) respondents stopped treatment with antidepressants altogether. A further 30 (9%) respondents reported that the patients stopped the medications themselves because of the warning. Another 67 (19%) either changed the dose and/or switched the medication. Six physicians stopped initiating treatment with antidepressants after the “black box” warning. Respondents also reported the emergence of several adverse events in teens treated with selective serotonin reuptake inhibitors (SSRI). The most commonly reported adverse events were agitation, aggressive behaviours, and headaches. There were also a few reports of worsening depression/suicidality, insomnia, and decreased appetite.

The survey suggests that many paediatricians are diagnosing depression and managing these cases with antidepressants in their practices. The response to the “black box” warning was not consistent. A large proportion of these paediatricians were aware of the FDA and Health Canada warnings from 2004 and reported changes in their practices according to the FDA recommendations (e.g., increased monitoring). Others stopped prescribing, changed doses or switched medications following the FDA and Health Canada notifications. The survey also indicated that Health Canada should develop a more efficient and effective system of communicating the importance of drug information with physicians.

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Congenital cytomegalovirus infection

January 2005

One of the many goals of the CPSP is to raise awareness and educate paediatricians about important conditions that may present in their patient populations. The program aims to support paediatricians in their diagnostic efforts so they will be able to both recognize and confirm the diagnosis of unusual, high-impact conditions. Education about diagnostic methods is particularly important when recommended diagnostic techniques have changed with the advent of new technology or new knowledge about the disease in question.

As the CPSP planned to embark on a new surveillance study of congenital cytomegalovirus (CMV) infection, one of the investigators' concerns was that paediatricians who see these cases infrequently may not be certain of the most appropriate diagnostic tests to perform. As the diagnosis is time sensitive, requiring isolation of the virus from the newborn in the first three weeks of life, it is critically important that front-line caregivers be aware of the most sensitive diagnostic method. Thus, an important goal of the study is to raise awareness of the most appropriate method for making the diagnosis of congenital CMV infection. Before the study began, a survey of current practice was undertaken as an educational and assessment tool.

The 2,472 participants were sent a one-time, single-question survey in January 2005, before the congenital CMV study began in March. Thirty-two percent (32%, n=786) of the participants responded and the results were encouraging. When asked to choose their preferred diagnostic test for a newborn with congenital CMV infection, the majority (69%) correctly chose a urine specimen or

a throat swab for CMV culture or polymerase chain reaction (PCR). However, another 25% indicated serology as their preferred diagnostic test.

The survey results were published as a CPSP Highlight in the August 2005 issue of *Paediatrics & Child Health*. The publication emphasized two important points:

- 1) The isolation of the virus or detection of viral DNA using PCR is a very sensitive and specific method of diagnosis, because there are massive quantities of CMV being excreted in the urine and saliva. CMV serology in the newborn is a poor way of identifying congenital CMV infection.
- 2) Although the presence of IgM is very specific for fetal and newborn infection, it is not very sensitive. Because the overwhelming infection occurs early on in gestation, the fetus does not mount a significant immune response and, in fact, develops immune tolerance for the virus.

Participants were encouraged to torch the serological TORCH screen, as detection of the virus is always best.

A follow-up survey is planned at the completion of the study to determine the educational benefit of CPSP participation for paediatricians.

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International adoption

September 2005

Canadian families have been adopting children internationally at increasing rates over the last 10 years with over 2,000 international adoptions annually. Most of these children are healthy. However, the majority are from countries and/or social situations with increased risks for specific infectious diseases acquired at birth or in the first years of life and where routine immunization is incomplete or inadequate. A one-time survey was included in the September 2005 CPSP mailing to determine the experience of Canadian paediatricians with children adopted internationally and their knowledge about current recommendations for screening these children for infectious diseases.

Responses were received from 665 (27%) of the 2,500 CPSP participants. Sixty-one percent (61%) of respondents cared for a child who had been adopted internationally within the previous two years. Among these, 59% cared for less than five children adopted internationally, 27.5% for five to 10 and 13.5% for more than 10. Screening frequency varied with disease: 79% had screened for hepatitis B, 73% for HIV, 71% for hepatitis C and tuberculosis, and 67% for syphilis. Together, these paediatricians identified 30 confirmed cases of hepatitis B, four of hepatitis C, four of syphilis, three of HIV and 111 infected with tuberculosis.

Knowledge about screening methods varied significantly and there were important gaps in knowledge, especially for hepatitis B. Contrary to expert recommendations, 35% of respondents indicated they wouldn't perform a tuberculosis skin test if the child had received a BCG vaccine.

The majority did not know that repeat screening is indicated six months after arrival in Canada for hepatitis B and C and HIV and within three to six months of arrival for tuberculosis. Most would consider repeating vaccinations but with incomplete knowledge about which serologic tests can be used to determine the need for this. However, an important minority (6%) would never revaccinate and seemed unaware of studies indicating that 20–40% of internationally adopted children lack immunity on serological testing to diseases against which they were reportedly vaccinated. There were no significant differences when analyses were restricted to those who had seen an internationally adopted child within the previous two years.

The majority of Canadian paediatricians who responded to the survey had recent experience with children who were adopted internationally. However, survey results point to a need for increased professional education to assist physicians caring for these children. Gaps in knowledge and practice may be leading to under-detection of conditions such as hepatitis B, hepatitis C and tuberculosis, putting children and their contacts at risk.

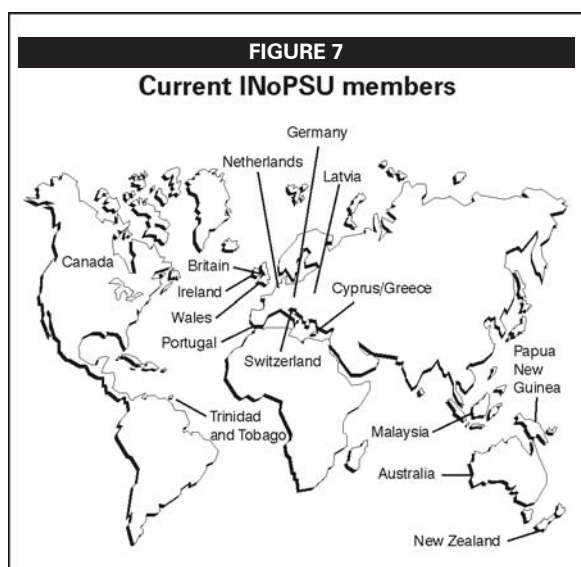
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International Developments

INoPSU

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 worldwide, there are 15 national paediatric surveillance units that are full members of INoPSU: Australia, Britain, Canada, Germany, Greece/Cyprus, 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, and Argentina is currently developing a surveillance unit.

The first formal INoPSU meeting was held in Ottawa in June 2000, with a second meeting in York, England, in April 2002. As a result of these successes, a third INoPSU meeting was held in Portugal in the spring of 2004. The fourth INoPSU conference will be hosted by the BPSU in London, England, in the spring of 2006.

Further information regarding all national paediatric surveillance units can be obtained on the INoPSU Web site at www.inopsu.com.

46th Annual Meeting of the European Society for Paediatric Research

Dr. Danielle Grenier and Sarah Srikanthan represented the CPSP at the European Society for Paediatric Research in Siena, Italy, August 31 to September 3, 2005. The scientific program



included new scientific developments in neonatology, neurology and nutrition, and their significance for paediatrics, with special emphasis on high-quality clinical research.

A poster on “Active surveillance of early-onset eating disorders, vitamin D deficiency rickets and Prader-Willi syndrome” was presented. The poster was well received, creating discussion about the presentation as well as the CPSP in general.

The conference proved beneficial, not only in promoting the impacts of surveillance to a much wider international audience, but also in building relationships with interested countries looking to form similar surveillance units. In particular, the Italian delegates expressed their interest in learning how to establish and run an active surveillance program. Time will tell whether Italy will join INoPSU, but from the initial interactions, future prospects look hopeful.

Highlights from other national paediatric surveillance units

Australia

Fetal Alcohol syndrome (FAS) was first identified in the 1970s and has been described as a preventable tragedy. FAS is caused by maternal alcohol consumption during early pregnancy and represents the most severe effects of exposure to alcohol in utero.

In January 2001, the Australian Paediatric Surveillance Unit (APSU) initiated surveillance for FAS, documenting 76 suspected or partial cases and an estimated incidence rate of 0.48 per 100,000 children less than 15 years of age. Over 60% of children reported were identified as indigenous.

Data from this study have been requested by decision-making bodies, including the Intergovernmental Committee on Drugs and the Ministerial Council on Drug Strategy. The data have also been disseminated in the media and through educational sources.

Studies under surveillance: *Acute flaccid paralysis, congenital cytomegalovirus infection, congenital rubella syndrome, early-onset eating disorders, haemoglobinopathy, hepatitis C virus infection, HIV/AIDS, hyperinsulinaemic hypoglycaemia of infancy, neonatal herpes simplex virus infection, neonatal/infant group B streptococcal sepsis, non-tuberculosis mycobacterial infection, Rett syndrome, vitamin K deficiency bleeding*

Britain

The British Paediatric Surveillance Unit (BPSU) has added the following three new studies this year: scleroderma, methicillin-resistant staphylococcus aureus (MRSA) and early-onset eating disorders (EOED). All three studies are using additional sources of ascertainment. For the EOED study, a new surveillance system has been set up to cover the 600 psychiatrists. To date, they have reported two-thirds of the cases and the response rate has been over 75%.

The forthcoming year will see the BPSU celebrate its 20th year of surveillance. Over the past 20 years, more than 60 conditions have been studied, more than 20,000 cases have been reported and more than 200 studies have published results. The response rate still remains over 90%, which is a true testament to the contribution of paediatricians in the United Kingdom and Ireland.

Studies under surveillance: *Childhood tuberculosis, congenital rubella syndrome, early-onset eating disorders, HIV/AIDS, Langerhans cell histiocytosis, medium-chain acyl-CoA dehydrogenase deficiency, methicillin-resistant staphylococcus aureus, neonatal herpes simplex virus infection, non-type 1 diabetes, progressive intellectual and neurological deterioration, scleroderma, severe hyperbilirubinemia, thyrotoxicosis*

Netherlands

The Netherlands Paediatric Surveillance Unit's (NSCK) study on preeclampsia includes data from gynaecologists. Preliminary study data identified a much higher incidence rate than in surrounding countries: 7.9 per 10,000 births compared to 4.9 per 10,000 births in the United Kingdom. The reason is unknown. Surveillance is ongoing to document the differences between countries.

Studies under surveillance: *Congenital malformations after maternal anti-epileptic drug use, diabetes mellitus, Down's syndrome, hemoglobinopathy, Henoch-Schönlein purpura, insufficient breastfeeding, nephrotic syndrome, shaken baby syndrome*

New Zealand

The New Zealand Paediatric Surveillance Unit's (NZPSU) major achievement was the publication of two surveillance papers. The first paper was entitled, "New Zealand national incidence of bronchiectasis too high for a developed country." The study prospectively estimated the incidence of bronchiectasis among children, described etiology and severity and evaluated regional and ethnic differences. The second paper entitled, "Prospective incidence study of diabetes mellitus in New Zealand children aged 0 to 14 years," looked to establish the incidence of type 1 diabetes in New Zealand's children. This study suggested that there has been a doubling increase of type 1 diabetes in New Zealand over the past 30 years.

Studies under surveillance: *Acute flaccid paralysis, congenital rubella syndrome, foregut and hindgut malformations, haemolytic uraemic syndrome, inborn errors of metabolism, perinatal HIV exposure, pneumococcal meningitis, prolonged infantile cholestasis, vitamin K deficiency bleeding*

Switzerland

Between April 2000 and March 2003, the Swiss Paediatric Surveillance Unit's (SPSU) study on varicella-zoster virus infections (VZV) documented 335 cases. Reports from the SPSU were verified for completeness of reporting by capture-recapture analysis with patient records identified by ICD-10 codes. Outcome of illness was assessed six months after hospitalization. The mean age of patients was 4.1 years (median 3.5 years, range 0–16 years). The clinical picture is shown in Table 28.

TABLE 28

Varicella-zoster virus infections study

Clinical picture	Number
Total cases	335
Hospitalization rate	13 per 104 cases
Diagnosis	
Chickenpox	293
Herpes zoster	42
Complications	319
Secondary bacterial infections	109
Central nervous system involvement	76
Varicella-zoster virus pneumonitis	7
Others	127
Sequelae	12

The results demonstrate a sizeable complication rate for VZV infections and provide a solid basis

for future immunization recommendations in Switzerland.

Studies under surveillance: *Acute flaccid paralysis, congenital rubella syndrome, acute rheumatic fever, haemolytic uraemic syndrome, intussusception, neonatal herpes simplex virus infection, neural tube defects, severe respiratory syncytial virus infections, shaken baby syndrome, vitamin K deficiency bleeding*

Wales

The Welsh Paediatric Surveillance Unit (WPSU) study on non-type 1 diabetes mellitus in Welsh children aims to determine the incidence of type 2 diabetes mellitus (T2DM) and the service implications for managing the potentially undiagnosed and increasing cohort. Preliminary data show that, of the 17 cases reported to date, seven were pubertal or post-pubertal and had a strong family history of type 2 diabetes. Steroid-induced diabetes occurred in four patients: one had acute lymphoblastic leukemia, two had renal disease, and one was a post-renal transplant situation. Four cases had maturity-onset diabetes of the young, one had cystic fibrosis-related diabetes, and the last one remained undiagnosed. Interestingly, 7/17 cases were Caucasian girls with T2DM, which differs from previous reports in the United Kingdom, where the majority of cases were South Asian or from Eastern backgrounds.

Studies under surveillance: *Adverse events from complementary and alternative medicine, complicated pneumonia including empyema, hypernatraemia in infancy, juvenile idiopathic arthritis, non-type 1 diabetes mellitus*

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

- 82% response from more than 2,400 paediatricians
- 93% data completion rate
- High duplicate reporting rate (18.6%) assuring case ascertainment and participant commitment

Study ideas

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

Biliary atresia	Childhood tuberculosis
Circumcision complications	Imported malaria
Congenital varicella	Brachial plexus injury
Familial melanoma	Methicillin-resistant <i>Staphylococcus aureus</i>
Sudden death in asthma	Severe hyponatremia
Heavy metal poisoning	Kawasaki disease
Histiocytosis disorders	Neonatal <i>Listeria</i> infections

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
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