



# CPSP

CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM



# 2006 RESULTS



Canadian  
Paediatric  
Society



Public Health  
Agency of Canada

Agence de santé  
publique du Canada



## **Mission Statement**

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

# CPSP 2006



2005 marked the CPSP's 10th anniversary celebration. This was an important landmark in a decade of active surveillance into high impact diseases and infections affecting children and youth in Canada.

In the spring of 2006, the program redesigned the CPSP Results publication and created a new CPSP logo. What does the new logo represent?

- The maple leaf represents Canada and the collaboration between the Canadian Paediatric Society and the Public Health Agency of Canada.
- The silhouette represents children and youth, targets of the program.
- The S symbol represents:
  - active surveillance,
  - the caduceus, symbol of the medical profession and the participating paediatricians,
  - the research path to improving the health of children and youth with rare diseases/conditions.

The CPSP website was relaunched to ensure easy navigation. The section on concluded studies includes information on investigators and concentrates on study results and related presentations and publications. The current study section includes case definitions and protocols. To facilitate early case reporting, the detailed questionnaire is available online in PDF format, so participants can easily download the form as soon as they see a case.

The publication section attests to the success of the program. Note the many national and international abstracts and oral presentations and the increasing number of published articles associated with the CPSP.

Over time, the program hopes to further develop the website to ensure easy retrieval of any information needed about the program. For ease of access, please mark the CPSP website in your web browser's *Favourites* and encourage your hospital web master to link with the CPSP website. Your feedback and suggestions are always welcome.

**[www.cps.ca/cpsp](http://www.cps.ca/cpsp)**





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# Acknowledgements

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

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

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

## Federal Minister of Health

As Minister of Health, I would like to congratulate and thank the Canadian Paediatric Society for the successful completion of the eleventh Canadian Paediatric Surveillance Program. The success of this program is due in large part to the contributions and support of paediatricians across Canada.

The Canadian Paediatric Surveillance Program is highly regarded throughout the international community. By monitoring relatively rare childhood diseases and conditions of public health importance, it helps make a difference in the lives of many Canadian families.

This is an important collaborative program for surveillance, research, and policy development. Canada's New Government will continue to work closely with the Canadian Paediatric Society, the provinces and territories, and other stakeholders to improve the overall health and well-being of Canadian children.



The Honourable  
Tony Clement

## Chief Public Health Officer of Canada

I am pleased to accept the eleventh annual report of the Canadian Paediatric Surveillance Program (CPSP). This program is highly regarded scientifically, and the data it produces generates action in the form of public health policy and standards of practice.

Through its Health Promotion and Chronic Disease Prevention Branch's Centre for Health Promotion, the Public Health Agency of Canada, partners with the CPSP on this initiative, as it complements very well the other maternal and child health surveillance activities of the Agency. Surveillance is a core public health function and is essential to evidence-based disease prevention and health promotion in children and youth.

On behalf of the Agency, I would like to sincerely thank all the paediatricians who contribute their time to the CPSP by completing detailed reports on each case.



Dr. David  
Butler-Jones

# President of the Canadian Paediatric Society

The Canadian Paediatric Society salutes the Public Health Agency of Canada for its commitment to funding the CPSP. As a paediatrician, I am honoured to introduce the CPSP 2006 Results.

The CPSP is familiar to all practising paediatricians for two major reasons. One is the ability to participate monthly in national collaborative epidemiological paediatric research that assists all of us in our daily practices. The other is the ongoing feedback paediatricians receive on the medical and public health impacts of the CPSP studies through the CPS News, the CPSP Highlights in the *Paediatrics & Child Health* journal and presentations in different venues.

The output of the CPSP is steadily growing and researchers have published study results in several peer-reviewed journals. The program has an international reputation, not only for its scientific study results, but also for demonstrating leadership in the comparative analysis of studies done simultaneously by several surveillance units from around the world.

As you can see, the CPSP is vigorous because paediatricians are dedicated to responding monthly. I would like to sincerely thank all of them for making the CPSP work. At the beginning of a second decade of surveillance, we are looking forward to successes in future years.



Dr. Robert  
Issenman

## CPSP Chairman

Once again, the CPSP has had a very busy and successful year.

The Canadian Paediatric Society and the Public Health Agency of Canada reaffirmed their commitment to the CPSP. The CPSP welcomes this vote of confidence and this renewed collaborative partnership.

As the CPSP Chairman, I would like to take this opportunity to encourage paediatricians to undertake an epidemiological surveillance study through the CPSP. Many areas of paediatrics could lend themselves to further research. Some studies will originate from paediatric subspecialties such as neurology, genetics and psychiatry, while others will be from the public health domain, such as the current studies on acute flaccid paralysis and head trauma secondary to child maltreatment. This tapestry is one of the strengths of the program and is essential to maintaining the active participation of all paediatricians.

The CPSP welcomes all, including community paediatricians, to submit their study ideas. Assistance is available to make the development of an application easier for future investigators.

Finally, I thank every single one of you who contributes monthly to the CPSP. Without you, this important epidemiological research for children and youth would not be possible.



Dr. Gilles Delage

# CPSP Steering Committee

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

## CPSP Working Group

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



A fond farewell to **Sarah Srikanthan**, Senior Coordinator, who returned home to New Zealand after two years of demonstrated commitment to the CPSP. We recognize her dedication and service, and we wish her well in her new endeavours.



# Publications in 2006



## Published papers related to studies

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

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

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

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

## Highlights published in *Paediatrics & Child Health*

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

Canadian Paediatric Surveillance Program Quiz. *Paediatr Child Health* 2006;11(10):692

Is the use of complementary and alternative medicine in the paediatric population safe? Survey results and next steps. *Paediatr Child Health* 2006;11(9):600

Unravelling the risk factors for non-type 1 diabetes in children. *Paediatr Child Health* 2006;11(8):506

The impact of antidepressants, adverse events warnings, and survey results. *Paediatr Child Health* 2006;11(7):455

International adoption evaluation challenges and survey results. *Paediatr Child Health* 2006;11(6):358

Public health impacts of CPSP Studies: 1996 to 2005. *Paediatr Child Health* 2006;11(5):286

Vomiting and fasting: Risky in infancy. *Paediatr Child Health* 2006;11(4):221

Respiratory distress... out of nowhere! *Paediatr Child Health* 2006;11(3):140

Hypotonia in a newborn: Unravelling more than expected. *Paediatr Child Health* 2006;11(2):106

A bump on the head: A simple fall or child maltreatment? *Paediatr Child Health* 2006;11(1):36



# Presentations in 2006

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

## National

Impact of surveillance on injury prevention. Grenier D, Doherty J, Srikanthan S. Canadian Association of Paediatric Health Centres Annual Meeting, Vancouver, in October.

Early-onset eating disorders. Pinhas L, Morris A, Heinmaa M, Crosby R, Katzman D. Canadian Paediatric Society Annual Conference, St. John's, in June.

Canadian incidence of Prader-Willi syndrome. Berall GB, Desantadina MV, Allanson J. Canadian Paediatric Society Annual Conference, St. John's, in June.

Impact of surveillance on injury prevention. Grenier D, Doherty J, Srikanthan S. Canadian Paediatric Society Annual Conference, St. John's, in June.

Incidence of acute rheumatic fever in Canadian children. Templeton CG, Dancey P, Human DG, Rahman P, Cooper AR. Canadian Paediatric Society Annual Conference, St. John's, in June.

Surveillance: Helping newborns with neurological challenges. Campbell C, Lee B. Canadian Paediatric Society Annual Conference, St. John's, in June.

A CPSP survey on Canadian paediatricians' experience and knowledge about the risks of infectious diseases in children adopted internationally. Hui C, Auger L, Baxter C, Chicoine JF, Clifford T, Embree J, Kahaler S, Kugelmass R, Kuhn S, Lawson M. Canadian Paediatric Society Annual Conference, St. John's, in June.

Incidence and cohort study of congenital DM. Campbell C, Levin S, Jacob P, Siu V, Venance S. Canadian Paediatric Society Annual Conference, St. John's, in June.

## International

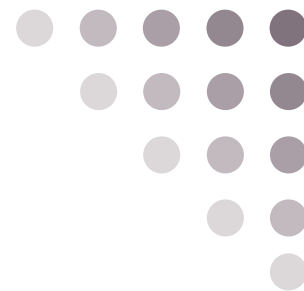
Neonatal diseases research through surveillance: The Canadian experience. Grenier D, Doherty J, Srikanthan S. European Academy of Paediatrics Congress, Barcelona, Spain, in October.

One-time surveys: CPSP added value. Grenier D, Doherty J, Srikanthan S. Fourth INoPSU Conference, London, England, in May.

International comparison of severe neonatal hyperbilirubinemia and herpes simplex virus infection. Grenier D, Doherty J, Sgro M, Manning D, Wong T, Jones C, Tookey P. Fourth INoPSU Conference, London, England, in May.

International comparison of WHO quality assurance criteria for acute flaccid paralysis surveillance. Grenier D, Doherty J, Srikanthan S. Fourth INoPSU Conference, London, England, in May.

# Funding



Funding for the CPSP is required to support program management. 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.

The CPSP is a collaborative program of the Canadian Paediatric Society and the Public Health Agency of Canada, with financial support from Health Canada.

We gratefully acknowledge the following organizations that have provided funding to the CPSP during part or all of 2006.

## 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
- Complementary and Alternative Research and Education Program
- Foresters
- Hema-Quebec
- The Hospital for Sick Children
- IWK Health Centre
- Janeway Children's Hospital Foundation
- Lawson Health Research Institute
- Manitoba Institute of Child Health
- Multiple Sclerosis Scientific Research Foundation
- Ontario Neurotrauma Foundation Prevention Committee
- William Singeris National Centre for Myotonic Dystrophy

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

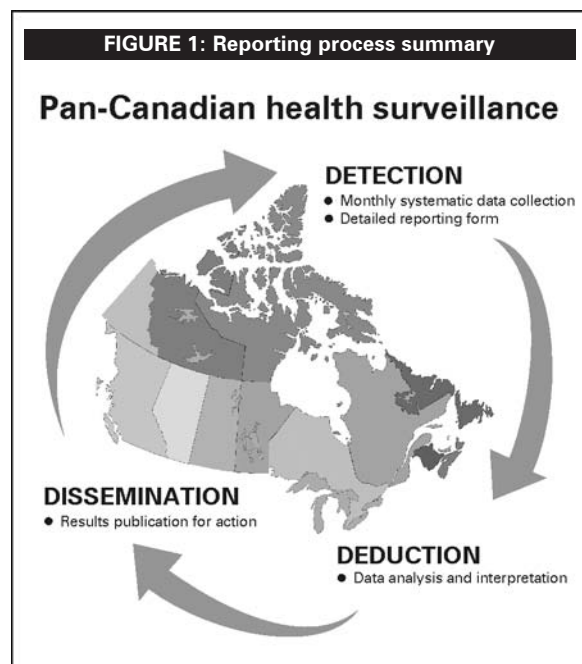
## Reporting

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

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

Confidentiality is maintained by using only non-nominal patient information, such as the date of birth, sex of the child and comments on the condition. This anonymous information is used to exclude duplicates and is sent to the original respondent to request case-specific information. Once the detailed questionnaire is returned to the CPSP, it is forwarded to the investigator for analysis. The investigator is responsible for contacting the respondent if further information is required.

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 78% national reporting rate (Table 1) and the 87% response rate for completion of detailed questionnaires (see Table 2 for study breakdown).

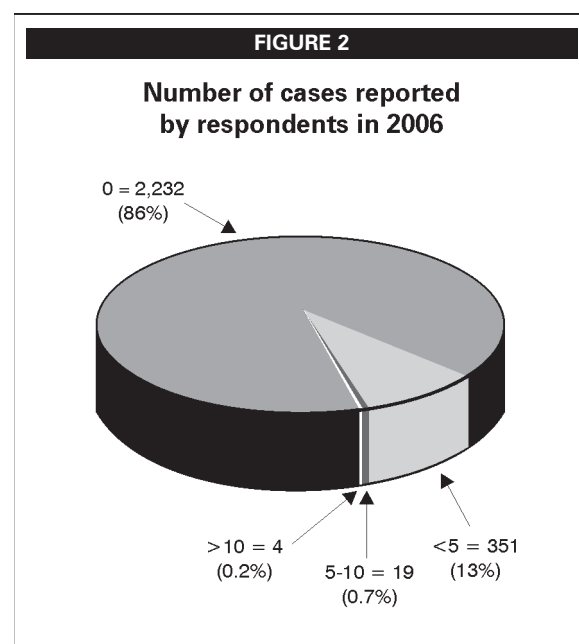
<b>TABLE 1</b>		
<b>Initial response rates (%) and number of participants for 2006</b>		
<b>Provinces/territories</b>	<b>Reporting rates (%)</b>	<b>Number of participants</b>
Alberta	78	277
British Columbia	76	258
Manitoba	81	123
New Brunswick	80	31
Newfoundland and Labrador	85	46
Nova Scotia	86	99
Northwest Territories	100	3
Nunavut	100	1
Ontario	79	971
Prince Edward Island	100	8
Quebec	76	658
Saskatchewan	64	48
Yukon	100	3
<b>Canada</b>	<b>78</b>	<b>2,526</b>

<b>TABLE 2</b>			
<b>2006 detailed questionnaire completion rates as of April 1, 2007</b>			
<b>Studies/conditions</b>	<b>Reported cases</b>	<b>Pending</b>	<b>% Completion rate</b>
Acquired demyelinating syndromes of the central nervous system	92	5	95
Acute flaccid paralysis	77	4	95
Acute rheumatic fever	36	8	78
Adverse drug reactions – serious and life-threatening	83	14	83
Congenital cytomegalovirus infection	45	4	91
Congenital myotonic dystrophy	31	4	87
Head injury secondary to suspected child maltreatment (abuse or neglect)	110	14	87
Medium-chain acyl-coenzyme A dehydrogenase deficiency	17	2	88
Non-type 1 diabetes mellitus	172	24	86
Severe combined immunodeficiency	13	4	69
Transfusion-related acute lung injury	3	2	67
<b>Total number of cases (all studies)</b>	<b>679</b>	<b>85</b>	<b>87</b>

## 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 2006, the majority of participants (82%) 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 2006. As studies come and go, the workload shifts to different subspecialties. The 2006 studies with the most reports were head injury secondary to suspected child maltreatment (abuse or neglect) and non-type 1 diabetes mellitus.



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, 1,695 personal certificates were sent to acknowledge CPSP participation in 2006,

and 322 letters of thanks went to participants who reported a case in 2006. In addition, Drs. Brenda Clark (AB) and Margaret Lawson (ON) were selected in this year's early-bird draw, each winning a dinner for two. The lucky winners of the year-end draws for complimentary registration for the June 2007 CPS Annual Conference in Montreal, Quebec, were Dr. Mahamadou Chaibou (NB), who responded for all months in 2006, and Dr. Michael Lester (ON), 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 2,606 participants. The program is committed to a case ascertainment rate of over 90% and, due to follow-up reminders to non-responders, obtains a response rate of 87% on detailed questionnaires (Table 2). The CPSP offers an opportunity for international collaboration with other paediatric surveillance units worldwide and a chance to make a difference in the health and 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 scientific and 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 website at [www.cps.ca/cpsp](http://www.cps.ca/cpsp) or contact the CPSP senior coordinator at [cpsp@cps.ca](mailto: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 2006 one-time survey question on adverse events associated with paediatric complementary and alternative medicine are found on page 44.

**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"> <li>• Name of principal investigator</li> <li>• Names of co-investigators</li> <li>• Brief abstract of proposal</li> <li>• Proposed starting date and duration</li> <li>• Specific study objectives</li> <li>• Statement of justification, including expected scientific and public health impacts</li> <li>• Case definition</li> <li>• Expected number of cases</li> <li>• Plan for ethical review</li> <li>• Funding arrangements</li> <li>• Identification of projected date for completion of analysis</li> </ul>

### Glossary of terms for tables of cases in each study results

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

## Studies timeline

**TABLE 5**

**CPSP studies timeline (by end date)**

Studies	Start date	End date	Total confirmed cases to December 31, 2006
Group B strep	January 1996	December 1996	178
Neural tube defects	January 1997	December 1998	107
Creutzfeldt-Jakob disease	January 1997	June 1999	1
Hemorrhagic disease of the newborn	January 1997	December 2000	6
Subacute sclerosing panencephalitis	January 1997	December 2000	3
Cerebral edema in diabetic ketoacidosis	July 1999	June 2001	23
Progressive intellectual and neurological deterioration	July 1999	June 2001	59
Anaphylaxis	January 2000	June 2001	732
Hemolytic uremic syndrome	April 2000	March 2002	140
Smith-Lemli-Opitz syndrome	January 2000	December 2002	35
Hepatitis C virus infection	February 2001	January 2003	58
Neonatal liver failure/perinatal hemochromatosis	February 2001	January 2003	10
Necrotizing fasciitis	September 2001	August 2003	37
Neonatal herpes simplex virus infection	October 2000	September 2003	58
Neonatal hyperbilirubinemia – severe	July 2002	June 2004	258
Vitamin D deficiency rickets	July 2002	June 2004	69
CHARGE association/syndrome	September 2001	August 2004	90
Congenital rubella syndrome	January 1996	December 2004	9
Prader-Willi syndrome	January 2003	December 2004	31
Early-onset eating disorders	March 2003	February 2005	160
Lap-belt syndrome	September 2003	August 2005	28
Osteogenesis imperfecta	January 2004	December 2005	27
Acquired demyelinating syndromes of the central nervous system	April 2004	March 2007	203
Acute rheumatic fever	April 2004	March 2007	54
Medium-chain acyl-coenzyme A dehydrogenase deficiency	September 2005	August 2007	10
Acute flaccid paralysis	January 1996	December 2007	442
Adverse drug reactions – serious and life-threatening	January 2004	December 2007	116
Congenital cytomegalovirus infection	March 2005	February 2008	37
Congenital myotonic dystrophy	March 2005	February 2008	12
Head injury secondary to suspected child maltreatment (abuse or neglect)	March 2005	February 2008	94
Severe combined immunodeficiency	April 2004	March 2008	15
Non-type 1 diabetes mellitus	April 2006	March 2008	110
Transfusion-related acute lung injury	September 2005	August 2008	2

## Survey questions

**TABLE 6**

**CPSP survey questions**

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



# CPSP Principal Investigators



## Surveillance studies in 2006



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



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



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



Dr. Shazhan Amed  
Non-type 1 diabetes  
mellitus



Dr. Ezzat Farzad  
Severe combined  
immunodeficiency



Dr. France Gauvin  
Transfusion-related  
acute lung injury





# Surveillance Studies in 2006



## Acquired demyelinating syndromes of the central nervous system

April 2004 to March 2007

### Highlights

- Demyelination is not as rare as previously thought, as 68 cases were confirmed in 2006.
- Four confirmed cases developed multiple sclerosis.
- Most of the 68 children with demyelination (71%) required treatment and 91% had a brain MRI performed.
- Reporting physicians discussed the possibility of recurrent demyelination with patients and families in 94% 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 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, 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

**TABLE 7**

**Acquired demyelinating syndromes of the central nervous system cases in 2006**

Reported	Duplicates	Excluded	Pending	Confirmed
92	16	1	7	68

#### Demographic and incidence data

There were 68 confirmed cases of demyelination reported in 2006. The majority of them were from Ontario (50%), Alberta (15%), Quebec (15%), British Columbia (8%) and Manitoba (6%). Four other provinces accounted for the remaining confirmed ADS cases. The mean age was 11 years (range 2.8–18.1 years) and the female to male ratio is 1.3:1 (39 females, 29 males).

#### Epidemiological and familial autoimmune data

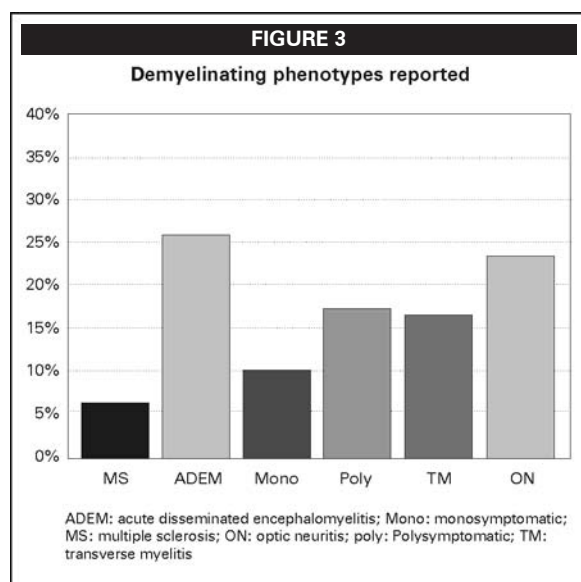
Most of the confirmed cases were born in Canada (89%), one was born in the United States and six children were born outside North America (Afghanistan, India, Cambodia, China, Colombia and Congo). The majority of patients reported European ancestry (56%). Other ancestries included Asian (6%), Middle Eastern (4%), Aboriginal (1%), Central and South American (3%), Caribbean (1%) and mixed-ancestry (16%). Ancestry was not recorded for seven patients. Ten percent (10%, n=7) of 68 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 (26%), followed by cases of optic neuritis (24%), polysymptomatic presentation (17%), transverse myelitis (16%), monosymptomatic presentation (10%) and MS (6%). Of the 16 optic neuritis cases, seven were documented as unilateral and nine were bilateral. Of the 12 polysymptomatic cases, six presented with a combination of both optic neuritis and transverse myelitis.

Treatment with corticosteroids or immune globulin for the demyelinating event was required for the majority of patients (71%). Combinations of corticosteroids and immune globulins were necessary for five patients.

Brain MRIs were performed in 62/68 cases (91%) and 49/62 (79%) reported abnormal white matter changes. Of the 13 patients without white matter changes, 11 had optic neuritis, one had transverse myelitis, and one had both optic neuritis and transverse myelitis. Ninety-six percent (96%) of the confirmed cases were first-time acute demyelinating syndromes and the risk of recurrent demyelination was discussed with the patients and families in 94% of these cases.



## Conclusion

On average, approximately six cases per month were reported in the first nine months of this study (April 1 to December 31, 2004), seven cases per month in the second year (2005) and six cases per month in the third year (2006). 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, when averaged over three years, and indicates that the incidence of ADS is nearly 76 cases per year.

The distribution of cases reported in each province has remained fairly consistent in 2005

and 2006. While case ascertainment was down by 8% in British Columbia, it increased by 8% in Eastern Canada. The consistent proportion of confirmed cases in 2005 and 2006 among all provinces demonstrates that, although ascertainment numbers were slightly lower in 2006 (68, as compared to 83 in 2005), awareness and recognition of paediatric demyelination remained high.

The majority of these patients required treatment for their demyelinating events and underwent brain MRI imaging. The proportion of children undergoing MRI has remained high (87% in 2004, 100% in 2005, and 91% in 2006). This most likely relates 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.

## Principal investigator

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# Acute flaccid paralysis

January 1996 to December 2007

## Highlights

- AFP detection rates continue to fall below global targets. However, duplicate reporting rates are high, suggesting there is good sensitivity in Canadian monitoring.
- The risk of wild poliovirus importation remains due to ongoing transmission in endemic and reinfected countries.
- Stool testing is essential to rule out poliovirus infection while ensuring that potential imported or import-related cases are rapidly detected.
- Reporting rates for 60-day follow-up status should be improved to document presence/absence of residual paralysis.
- AFP surveillance continues to be an important activity for documenting Canada's polio-free status.

## Background

Elimination of indigenous wild poliovirus transmission was certified in Canada, and the rest of the American region, 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 for importation of wild polioviruses. Outbreaks of polio are presently occurring in four endemic and several newly reinfected regions in Africa and Asia (see [www.polioeradication.org](http://www.polioeradication.org) for current country-specific case counts). Consequently, active surveillance with appropriate follow-up investigation of acute flaccid paralysis (AFP) in children less than 15 years of age continues to be used to monitor for potential cases of paralytic poliomyelitis. This important activity is Canada's safeguard in maintaining vigilance for potential import or import-associated cases of paralytic poliomyelitis.

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

The expected background annual incidence for AFP in the absence of wild poliovirus transmission is one AFP case per 100,000 of the population aged less than 15 years. This equates to between 57 and 60 cases per year in Canada. AFP

surveillance is conducted jointly through two paediatric surveillance networks in Canada: the IMPACT (Immunization Monitoring Program, ACTive) network of paediatric tertiary care centres, who initiated AFP surveillance in 1991; and the CPSP, who implemented case detection and documentation in 1996. This report presents the results of AFP surveillance in 2006, 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 (including Guillain-Barré syndrome [GBS]) per year for every 100,000 children less than 15 years of age.
- 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 were 77 reports of AFP during 2006, including 27 confirmed cases. Over half (57%) of the reports were submitted by the CPSP and the remainder by IMPACT. Two-thirds of the detailed questionnaires were submitted from IMPACT hospitals. The majority (74%) of confirmed cases, were reported from three provinces (ON, AB and QC) and may have included cases transferred from other provinces or territories into the reporting province.

**TABLE 8**

### Acute flaccid paralysis cases in 2006

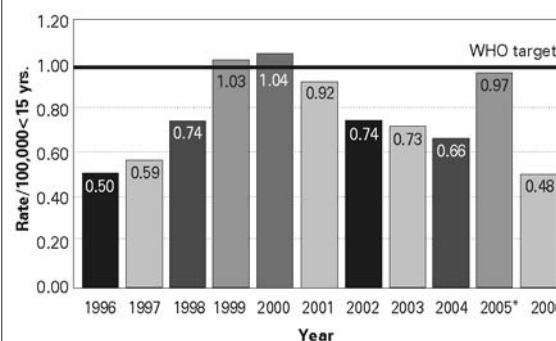
Reported	Duplicates	Excluded	Pending	Confirmed
77	38	8	4	27

Eight reports were excluded: six based on age criteria (for children over 15 years) and two based on another diagnosis explaining the paralysis (infantile botulism for one and vascular trauma preceding onset of paralysis for the other). The 27 confirmed cases for 2006 represent a non-polio AFP detection rate of 0.48/100,000 children under 15 years of age. This is below the 1/100,000 per year expected rate. However, the number of cases captured multiple times by the CPSP and IMPACT was high, with an average of two reports for each confirmed case. As in previous years, the number of confirmed cases and the annual AFP incidence rate may be artificially low due to delays in receiving detailed questionnaires, four of which are still pending (Figure 4).

In 2006, AFP cases ranged in age from 11 months to 14 years (median 7.4 years, mean 7.7 years). Table 9 shows the age distribution of AFP cases since 1996. As in previous years, cases reported in 2006 were fairly evenly distributed across the age groups. The male to female ratio has varied over the years with no clear pattern, which may be a result of the small overall number of cases resulting in a slight preference for one sex or the other in different years. In 2006, there were 1.2 male cases for every female case reported.

**FIGURE 4**

### Non-polio AFP detection rate, Canada 1996-2006



\* Includes nine delayed reports not included in the CPSP 2005 Results

Only 13 (48%) AFP cases had detailed documentation of routine childhood immunization. Of these, 11 had received age-appropriate polio immunization with inactivated poliovirus vaccine (IPV). An additional six cases had polio vaccination information reported as “up-to-date” but with no accompanying vaccine or date details and three other cases were born or travelled abroad and had documented vaccination with oral polio vaccine (OPV) or a combination of OPV and IPV doses.

**TABLE 9**

### Age distribution of AFP cases reported to the CPSP

Age group (yrs)	Number of cases										
	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005*	2006
0-1	2	–	2	3	2	8	10	5	5	8	3
2-5	11	13	15	18	24	18	16	17	15	20	8
6-10	9	12	18	23	22	14	11	7	10	14	7
11-14	8	10	9	17	13	14	6	15	8	13	9
<b>Total</b>	<b>30</b>	<b>35</b>	<b>44</b>	<b>61</b>	<b>61</b>	<b>54</b>	<b>43</b>	<b>44</b>	<b>38</b>	<b>55</b>	<b>27</b>

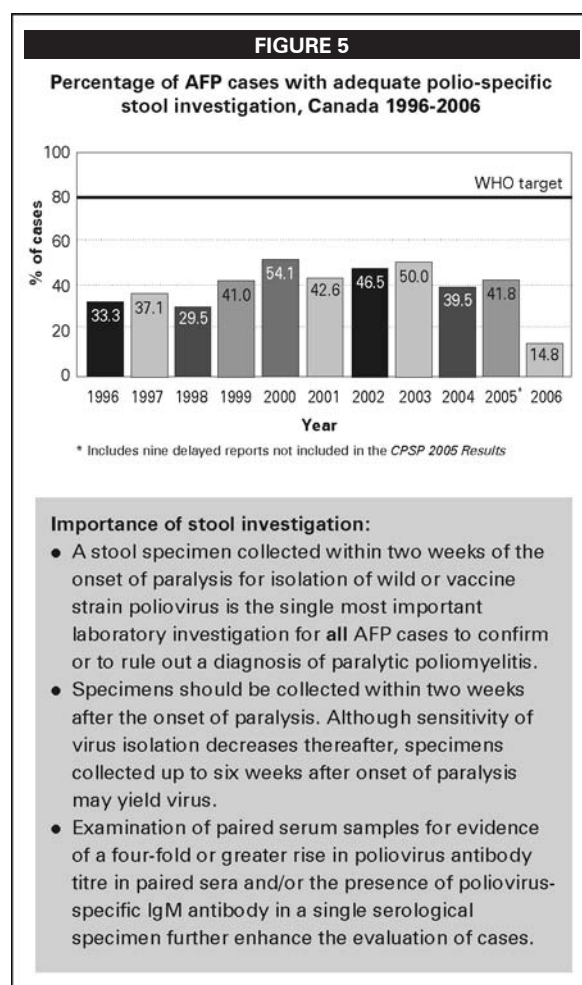
\* Includes nine delayed reports not included in the CPSP 2005 Results

## Virological investigation for polio or other enteroviruses

Virological investigation of AFP cases included collection and testing of stool specimens for seven cases (26%), cerebrospinal fluid (CSF) for 16 cases (59%), throat swabs for 15 cases (56%) and polio-specific serology for one case (4%). Although



stool was collected for virological investigation for seven cases, only four (15%) had adequate investigation for isolation of poliovirus or non-polio enteroviruses within two weeks of the onset of paralysis. For the remaining three cases (11%), two were missing stool specimen collection dates and one had stool collected after two weeks of the onset of paralysis, when the sensitivity of virus isolation is decreased. There were two instances where stool collection was requested but was not done. Over the past 10 years, rates of adequate stool investigation have been consistently below the WHO surveillance target (80% of cases) with a low of 15% for polio-specific stool testing in 2006 (Figure 5). While there was no positive identification of polioviruses from any of the virological investigations, another viral etiology was identified in three cases (mononucleosis, mycoplasma infection and influenza B).



### Campylobacter investigation

*Campylobacter* stool culture was added to the AFP surveillance study in 2001 to explore possible links between campylobacter infection and GBS. Testing for *Campylobacter* increased from 24% of cases in 2005 to 33% in 2006. No tests were positive for *Campylobacter*. Given the short period and the relatively low number of cases investigated each year, it is not possible to draw any conclusions regarding campylobacter infection and the development of GBS.

### Neurological investigations

Neurological investigations consisted of at least one of CSF examination, nerve conduction studies, electromyography, or MRI or CT scan. In 2006, CSF chemistry was the most frequently used neurological investigation (n=24 cases, 89%), showing abnormalities in 22/24 cases (92%). Electromyography and/or nerve conduction studies remained the second most frequently used (n=21 cases, 78%), showing abnormalities in 18/21 cases (86%). MRI or CT scans were least often used (n=20 cases, 74%), showing abnormalities in 6/20 cases (30%).

**TABLE 10**  
Neurological diagnosis of AFP cases, Canada

Diagnosis	Number of cases										
	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005*	2006
Polio	0	0	0	0	0	0	0	0	0	0	0
Guillain-Barré syndrome	21	29	34	50	49	42	33	33	27	36	23
Transverse myelitis	6	2	6	7	4	8	7	4	7	10	2
Other†	2	3	1	4	8	4	3	7	4	9	2
Not specified or undetermined	1	1	3	—	—	—	—	—	—	—	—
<b>Total</b>	<b>30</b>	<b>35</b>	<b>44</b>	<b>61</b>	<b>61</b>	<b>54</b>	<b>43</b>	<b>44</b>	<b>38</b>	<b>55</b>	<b>27</b>

\* Includes nine delayed reports not included in the CPSP 2005 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

As observed in previous years, the majority of AFP cases (n=23 cases, 85%) were diagnosed as GBS, two of which were Miller-Fisher variant. However, there

were only two diagnoses of transverse myelitis/post-infectious inflammatory myelitis reported in 2006 compared to an average of six reported in previous years (range 2–10 per year). The remaining two “other” cases included idiopathic Bells Palsy and peripheral neuropathy secondary to mycoplasma infection (Table 10).

### ***Hospitalization and outcome***

All but one (26/27, 96%) of the AFP cases in 2006 required hospitalization, with lengths of stay ranging from one to 39 days (average 14 days). Outcome at the time of the initial report was documented for 25 cases (93%) including: five cases (20%) fully recovered, 17 cases (68%) partially recovered with residual weakness or paralysis and three cases (12%) not recovered but condition reported as progressing. Only eight cases (33%) had status at 60 days reported, including five cases fully recovered, one partially recovered with residual weakness or paralysis, one with outcomes pending and one death. This is below the 80% WHO recommended target for high quality AFP surveillance and may be related to the timing of report completion/submission.

### **Conclusion**

The total of 27 AFP cases identified to date for 2006 is less than the expected number and consequently Canada’s non-polio AFP detection rate of 0.48/100,000 remains below the WHO target of 1/100,000 for 2006. This target has been met only twice (in 1999 and 2000) since AFP surveillance began in 1996. This is despite seemingly sensitive surveillance and the detection of confirmed cases through both the CPSP and IMPACT networks. In 2006, the largest ever number of late reports were received for cases with onset in the previous reporting year. Nine confirmed AFP cases, with onset in 2005, had detailed questionnaires submitted in 2006. These late reports represented 16% of the 2005 case reports, elevating the AFP detection rate to the highest seen in the previous five years (0.97/100,000). Nevertheless, Canada’s lower than expected AFP rates may be a result of under-detection of cases or alternatively they may be a true reflection of lower baseline levels for

non-polio AFP in Canada and other developed countries.

The vast majority of AFP cases continue to undergo one or more neurological investigations. 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. 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 can be investigated through prompt virological investigation of stool or other clinical specimens. Negative results of appropriate polio-specific investigations are as important as a positive results in AFP case evaluations.

The quality of Canadian AFP surveillance could be improved through increased stool sampling and virological testing for polioviruses and non-polio enteroviruses. In addition, improving documentation of 60-day follow-up with observation of any residual paralysis and timely completion and submission of detailed questionnaires would increase the quality of our AFP surveillance and documentation.

Despite some continuing challenges, global polio eradication was reaffirmed by the Advisory Committee on Polio Eradication (Geneva, 2005) and at the World Health Assembly (Geneva, 2006). While almost 2,000 cases of poliomyelitis were reported globally in 2006, 94% of these cases occurred in four countries where indigenous polio transmission is still occurring: Nigeria, India, Pakistan and Afghanistan. Of the over 20 polio-free countries that have been reinfected since 2003, 13 reported poliomyelitis cases in 2006. Eradication efforts in 2007 will focus on curbing intense transmission in the high-priority states of northern Nigeria and western Uttar Pradesh, India. With reinfection of several polio-free

countries, including some African countries with close ties to the Americas, the Pan American Health Organization emphasizes that the Americas remain at constant risk of polio importations. All countries, including Canada, must maintain high quality AFP surveillance and high vaccine coverage to prevent reinfection.

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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: 10 children with polyarthritis and four each with carditis and Sydenham's chorea.
- Multiple medication needs are documented.
- Vigilance is important in the prevention of ARF.

## Background

Acute rheumatic fever is a post-infectious collagen vascular disease affecting the heart, joints and central nervous system. It follows untreated Group A streptococcal (GAS) pharyngitis after a latent period of approximately three weeks. It does not occur after other GAS infection, such as skin infection (impetigo). Worldwide, it remains the 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 acute rheumatic fever in developed countries has decreased dramatically since its last peak in the 1970s, but it has not disappeared, and remains an important public health issue. The reason for its decrease is not fully understood. The decline in incidence in the early 20<sup>th</sup> century had already begun prior to the introduction of effective antimicrobial agents, but common use of penicillin to treat symptomatic sore throat may have contributed to the decline somewhat. Socioeconomic factors such as overcrowding and low income are known to be significant risk factors. The majority of cases of rheumatic fever follow cases of pharyngitis due to specific M serotypes of GAS, most commonly 1, 3, 5, 6, 18, 19 and 24. Spontaneous fluctuation of the prevalence of these serotypes is known to occur.

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

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

There is no current Canadian literature to suggest incidence. This is a sufficiently rare condition 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 11).

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 11**

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

Major manifestations	Minor manifestations
Carditis Polyarthrititis 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

The 16 cases confirmed in 2006 were from six provinces (AL, SK, MB, ON, QC, and NL). The gender distribution was approximately equal with nine males and seven females. The average age at diagnosis was 11.1 years.

**TABLE 12**

**Acute rheumatic fever cases in 2006**

Reported	Duplicates	Excluded	Pending	Confirmed
35	5	4	10	16

### Systems affected

Four patients had carditis meeting clinical criteria, and all of them required ongoing medical therapy at the time of reporting. Therapy consisted of ACE inhibitors in three cases and inotropic support in one. This last case also required surgical therapy, with mitral replacement and aortic repair. Ten patients had polyarthrititis meeting clinical criteria. Three had ongoing need for anti-inflammatory medication at the time of reporting. Agents used were naproxen and ibuprofen. Four patients had

Sydenham's chorea, and three required medical therapy. Agents used were pimozide, resperidone and haloperidol. One patient was reported with subcutaneous nodules, and another one with erythema marginatum. No mortality was reported.

### Long-term prophylaxis

All 16 children are receiving long-term prophylaxis against streptococcal infection. One is receiving monthly intramuscular injections of benzathine penicillin and the remaining fifteen are receiving oral penicillin twice daily.

## Conclusion

The third year of the ARF study has shown results consistent with the first two years, with a very small number of cases reported nationally (16 cases in 2006, 20 cases in 2005 and 18 cases in 2004). These results confirm that ARF 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 it is prevented whenever possible.

It is hoped that ultimately the ARF study will provide valuable data on the incidence of rheumatic fever so that this can be taken into consideration in guidelines for treatment of pharyngitis, keeping the relevant risks balanced.

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# Congenital cytomegalovirus infection

March 2005 to February 2008

## Highlights

- The study confirmed 19 cases of congenital CMV in 2006.
- Three infants died for an early mortality rate of 8%.
- Infants are often severely affected and diagnosed prenatally.
- All reported infants were diagnosed by viral isolation or molecular diagnostics.

## Background

Congenital cytomegalovirus infection (CMV) 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; 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, there is minimal Canadian epidemiological data, which is at least 25 years old. Current data specific to our own population is essential in 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 (NIH) 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. This 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 on a national sampling of the paediatric population.

## Objectives

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

## Case definition

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

- culture of CMV from an appropriate clinical specimen\*
- polymerase chain reaction (PCR) positive for CMV from an appropriate clinical specimen\*
- presence of CMV-specific IgM in the neonatal or cord blood†

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

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

## Results

There were 43 reports received in 2006: 19 from Ontario, 11 from Quebec and the remaining 13 reports were from six provinces (BC, AB, SK, MB, NS and NL). Of the 26 completed detailed questionnaires, 19 CMV cases were confirmed and seven 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. This delay in testing occurs either because the diagnosis is 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. Eight detailed questionnaires have not been returned as of this report.

**TABLE 13**

**Congenital cytomegalovirus infection cases in 2006**

Reported	Duplicates	Excluded	Pending	Confirmed
43	9	7	8	19

### Cumulative results form March 2005 to December 2006

#### *Demographics and epidemiological data*

There were 37 confirmed CMV cases out of 82 reports. The majority were from Ontario (n=32), followed by Quebec (n=18), Alberta (n=8), British Columbia (n=6) and New Brunswick (n=6). The remaining 12 reports were from four provinces (SK, MB, NS and NL). No reports were received from Prince Edward Island or the territories.

Four of the confirmed cases (11%) were from rural areas (population < 1,000); three of these rural cases were born to First Nations women. Maternal ethnicity was as follows: Caucasian (51%), Asian (16%), First Nations (14%), Black (5%), Latin American (3%) and unknown (11%). Of the 37 confirmed cases, 28 of the mothers were born in Canada, five were born outside the country (one immigrated more than five years before, three immigrated between one to five years before) and four were unknown. Mothers (n=32) had a mean age of 24.5 years (range 16–41 years) and 21 were primiparous.

## Clinical Presentation

Twenty-one (57%) of the congenitally infected infants were diagnosed prenatally: two by maternal serology only and 19 by fetal imaging showing either IUGR or cranial abnormalities. One of these infants was a stillbirth and the diagnosis, which was suspected as a result of fetal imaging (showing intracranial calcifications, severe IUGR and hydrops) and maternal IgM, was confirmed by amniotic fluid PCR (which is fetal urine). 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 (n=37) were diagnosed with a urine test positive for CMV, 33 by viral culture and five by PCR. One infant was diagnosed prenatally with amniotic fluid PCR. Newborn IgM serology was positive in only eight of the infected infants, it was negative in five, not done in 15 and unknown or missing in nine cases.

## Management

Most of the infants had some form of cranial imaging, including head ultrasounds (n=32) (abnormal in 17, normal in 15), cranial MRI or CT scans (n=18) (abnormal in nine, normal in nine). Hearing assessments were carried out on 25 infants (abnormal in eight, normal in 16 and done without result in one). Ophthalmologic assessments were carried out on 29 infants (abnormal in five, normal in 23 and done without result in one). Of the reported infants, 10 received intravenous ganciclovir therapy. All of these infants had significant neurological symptoms, usually including abnormal cranial imaging. Infected infants remained in the reporting hospital a total of more than 749 days (paediatricians sometimes reported the length of stay at their hospital only, before the infant was transferred to a tertiary care centre). Most infants were admitted to the neonatal intensive care unit for a mean stay of 25 days (range 3–71 days). One infant was a stillbirth, one died at 27 days, and one died at eight weeks for an early mortality rate of 8%. The rest were discharged home or transferred to another facility during the reporting period and the final outcome is not known.

## Discussion

Thus far, the surveillance study confirmed 37 cases of congenital CMV. The current rate of congenital CMV infection in Canada is not yet known. If the rate was 1%, with 10% of these infants being symptomatic in the newborn period, there should be approximately 300 cases per year for the Canadian birth cohort. The relatively low number of reports may reflect a number of factors, such as: 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 through the CPSP to estimate the reporting rate for diagnosed cases); and neonatal symptoms may be subtle and not recognized as congenital CMV early enough in the neonatal period to make a definitive diagnosis. The most accurate measurement of the infection rate will likely have to await population-based surveillance to capture the full spectrum of congenital CMV in Canada. Comparisons of infection rates detected by the CPSP and population-based screening will be important data with which to assess the need for implementation of population-based routine screening for congenital CMV.

More than half of the cases (57%) presented prenatally with most showing abnormal fetal ultrasound (usually of the brain) and these infants were severely affected. This emphasizes that infants diagnosed in the neonatal period may represent the “tip of the iceberg” and less severely affected infants may be missed for diagnostic purposes but still have significant neurological sequelae which remain undiagnosed. Such sequelae, deafness in particular, may be recognized late and intervention

is delayed. First Nations and new Canadian children appear to be at higher risk of congenital CMV infection. Seventy-five percent (75%) of infected children born in rural Canada were of First Nations origin. This observation will await further analysis with data from the complete study.

Viral isolation or PCR confirmed the diagnosis from the urine in all 37 cases. Neonatal IgM (as performed by the “TORCH” screen) had a low sensitivity. Only 61% of those tested were positive and 65% of cases did not have the test performed. The low rate of serological testing may be a result of the pre-study survey and educational intervention with CPSP participants.

Congenital CMV caused significant morbidity during the neonatal reporting period with affected infants experiencing prolonged hospital stays of high intensity and with 27% receiving intravenous ganciclovir therapy. Three infants died for an early mortality rate of 8%. This early, severe morbidity and mortality likely represents only a small fraction of the true burden of congenital CMV disease in Canada.

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# Congenital myotonic dystrophy

March 2005 to February 2008

## Highlights

- Eight confirmed cases were seen in 2006, in keeping with initial estimates.
- Three cases of prolonged ventilation (>20 days) were reported in 2006 with two of these children dying.
- The variability between genotype and phenotype and the number of children reported as index cases remains high.

## Background

Myotonic dystrophy is an autosomal dominant multi-system disorder characterized by muscle weakness and myotonia commonly beginning in adulthood. There are now three genetic loci for the disease but only one of these, DM1, is associated with a congenital form of myotonic dystrophy (CMD). The DM1 mutation is a CTG trinucleotide repeat in the DMPK gene on chromosome 19q13.3. Although the disruption of the DMPK protein may contribute to the symptoms of the disease, the primary pathogenesis is felt to be related to the impact of large accumulations of nuclear mutant mRNA on protein splicing. 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 cases 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 31 cases reported between January 1, 2006 and December 31, 2006. Of these, eight cases met the inclusion criteria and were diagnosed and reported in five different provinces across Canada. There were six females reported. The children were all diagnosed in the newborn period except one who was diagnosed at two years of age but had both respiratory and feeding difficulties requiring prolonged neonatal admission which was never explained at that time. This child has had recurrent pneumonia and mild developmental delay. The number of CTG repeats ranged from 1,100 to 2,300.

**TABLE 14**

**Congenital myotonic dystrophy cases in 2006**

Reported	Duplicates	Excluded	Pending	Confirmed
31	9	7	7	8

Three of the confirmed CMD cases died while in hospital at one, 24 and 26 days respectively. Two of the deceased cases had genetic confirmation of CMD with trinucleotide repeats of 1,100 and >2,000. The third deceased case did not have genetic confirmation of CMD; rather, this diagnosis was based on symptoms at birth and maternal genetic diagnosis of DM1.

All eight children had hypotonia and feeding difficulties that led to prolonged hospitalization. The duration of hospital admission ranged from one to at least 79 days, with the shortest length of admission not attributable to death being 21 days. Seven (7/8) cases required assisted ventilation with an average duration of 25 days (range 1–60 days). No follow-up data is available on one child

who was still ventilated at 24 days upon transfer to another hospital. Of these seven children, three died, one due to *Klebsiella pneumoniae*, one to rapid respiratory deterioration, and one due to withdrawal of supportive care at 24 days. The other four living children needing ventilation had trinucleotide repeat expansions of 1,300, 1,200, 1,300 and 2,300 respectively. Presently, information is available on only one child in the study who has had prolonged ventilation (60 days) and has been able to come off the ventilator and discharged home. This child needed CPAP and plication of the right hemi-diaphragm to facilitate adequate independent ventilation. All the ventilated children also experienced feeding difficulties. For three of these children, feeding dysfunction prolonged their hospital stays and was the primary reason they remained in hospital following extubation.

Half (4/8) of the children were the index cases for their families. In the other half, the mother had a known diagnosis. Only one of these cases received specific prenatal counselling about the risk of transmission to a child and the phenomenon of genetic anticipation.

Three children have agreed to join the national cohort study, three could not join as they died early, and in the final two cases we are awaiting agreement to join the cohort. Updates on the CPSP study and the cohort study have been presented at the 5<sup>th</sup> International Myotonic Dystrophy Consortium in 2005 and the Canadian Paediatric Society Annual Conference in 2006. Updates will also be presented at the Canadian Neuroscience Federation Meeting in June 2007.

## Conclusion

The CMD surveillance confirmed 12 cases in the first 22-month period, which represents slightly fewer cases than the expected 10–12 per year. However, at the current time there are seven cases under review and initial indications suggest that the majority of these will become confirmed cases.

Thus far, for the complete study period ending December 2006, reported children have had a wide range of phenotypes with feeding difficulties

being the main cause of prolonged admission in the newborn period. In total, eight children have required ventilation. Four (4/8) cases required prolonged ventilation, with two children dying at approximately one month of age, while still on a ventilator. The genotype-phenotype variability continues to be high. Two children with a similarly high number of trinucleotide repeats (>2,000) showed widely divergent clinical courses with one dying and the second only needing a short ventilation and hospital stay. Additionally, one of the other children who died had one of the smallest repeat sizes (1,100).

Ongoing surveillance over the coming years will be important for drawing more firm conclusions from the 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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# Head injury secondary to suspected child maltreatment (abuse or neglect)

March 2005 to February 2008

## Highlights

- In 2006, the study on head injury secondary to suspected child maltreatment confirmed 51 cases.
- Shaken baby syndrome was the suspected diagnosis in 67% of the cases reported.
- Injuries resulted in three deaths and 40% of the cases had mild to severe neurological sequelae.
- Child welfare authorities had previously been involved in 38% 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 they follow to protect those children.

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

Attempts have been made to quantify the issue in Canada; however, the information is limited. One effort was a time-limited study examining only

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

## Objectives

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

## Case definition

Report all new cases of a child up to 14 years of age inclusively, who has any mechanism of head or brain injury consistent with abuse/neglect\* (e.g., shaking, impact, suffocation) and that 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 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 51 cases confirmed to date in 2006, 16% were from the Western provinces (BC, AB, SK and MB), 82% were from Central Canada (ON and QC) and 2% were from Eastern Canada. The median age at initial presentation was five months (n=46, range 1–23 months). There were 32 boys, 17 girls and the gender of two children was unknown. Of those cases where numbers of children in the household were reported (92%), the median number of children was two (range 1–8).

**TABLE 15**

**Head injury secondary to suspected child maltreatment cases in 2006**

Reported	Duplicates	Excluded	Pending	Confirmed
110	31	3	25	51

### Management

Of the confirmed cases, 80% 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 0–365).

The initial presentation included soft tissue injury (35%), irritability (33%), lethargy (31%), vomiting (29%), seizure (29%), decreased consciousness (26%), apnea (14%) and respiratory difficulty (8%). All 51 confirmed cases were hospitalized. Data on length of stay were available for 43/51 cases, with a median length of stay of nine days (range 1–63 days). Almost half (45%) of the cases were admitted to the intensive care unit (ICU). Data on length of stay in the ICU were available for 12/43 cases, with a median length of stay of six days (range 1–14 days). A hospital child protection team was involved in 46/51 (90%) of the cases and the police were involved in 45/51 (88%) of the cases. Of the 45/51 confirmed cases with available information, child welfare authorities had previously investigated 17/45 cases (38%).

### Injuries

Clinical findings were found in 48/51 cases and included:

- Subdural hematoma (65%)
- Retinal hemorrhage (53%)
- Skull fractures (51%)
- Bruising (41%)
- Seizures (35%)
- Focal neurological findings (24%)
- Cerebral edema (22%)
- Subarachnoid hematoma (22%)
- Fractures of long bones or ribs (18%)
- Cerebral contusion (18%)
- Abrasions (10%)
- Epidural hematoma (10%)
- Abdominal injuries (4%)

Previous medical history was reported for 17 of the cases and the most frequent issues were a premorbid condition, previous maltreatment, excessive crying, prematurity (<36 weeks) and colic. SBS was the suspected diagnosis in 67% of the cases while other suspected physical abuse accounted for 26% and suspected neglect for 8%. Medical status at time of discharge was available for 45 cases. In three of these cases (7%) the injuries resulted in death and in 18 cases (40%) there were mild to severe neurological sequelae.

### Perpetrator

Perpetrator status was confirmed in nearly 14% of cases, suspected in 31% and unknown in

55%. In 16/23 cases, the confirmed or suspected perpetrator was a male and in 11/23, the confirmed or suspected perpetrator lived with the child. The relationship of the confirmed or suspected perpetrator to the child and a history of risk factors were available for 20/51 cases. The confirmed or suspected perpetrator was a parent in 75% of these cases, followed by the babysitter (10%). Half of the confirmed or suspected perpetrators (10/20) had a history of at least one risk factor, with the most common risk factors being domestic violence, few social supports, and drug and alcohol abuse.

## Conclusion

Results from the second year of this study have shown that head injury secondary to suspected child maltreatment (abuse or neglect) in children up to 14 years of age continues to be prevalent in our society with 51 cases confirmed at a median age of five months, and two-thirds of those diagnosed as suspected SBS. There were significant mortality and morbidity among confirmed cases. In the 51 cases where the outcome was known at the time of discharge, 7% resulted in death and 40% had mild to severe neurological sequelae.

All health care providers have to keep a high index of suspicion to diagnose affected children. With 80% of reported cases presenting to an emergency

department, there is also a need for adequate clinical preparation of health care providers in the identification of these cases. The fact that the child welfare authorities had previously been involved in over one-third (17/45) of cases with available information reinforces the importance of support and close follow-up of the families. Thus far, the findings are quite consistent and confirm that this study will provide data that can inform educational efforts to improve recognition of these cases by health care professionals and should hopefully lead to more effective prevention efforts.

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# Medium-chain acyl-coenzyme A dehydrogenase deficiency

September 2005 to August 2007

## Highlights

- Nine cases of MCAD deficiency were confirmed in 2006.
- All diagnosed patients were asymptomatic and detected in provinces with screening programs.
- Newborn genetic screening is ongoing in BC, SK, ON, NB, NS, PE, NL and YK.

## Background

Medium-chain acyl-coenzyme A dehydrogenase (MCAD) deficiency is the most common autosomal recessive inherited fatty acid oxidation disorder with an incidence of about one in 10,000–20,000. MCAD is one of the enzymes involved in the fatty acid beta-oxidation pathway. The 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 also 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 octanoylcarnitine) 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. With the advent of newborn screening and the use of tandem mass spectrometry, this disorder is now being screened for in the neonatal period in a number of countries, including a number of American states and seven Canadian provinces and one territory (BC, SK, ON, NB, NS, PE, NL and YK). 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. The exact incidence of MCAD deficiency in Canada is still largely unknown due to the lack of universal 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 to C10 acylcarnitines with predominance of C8 (octanoylcarnitine);
- 2) elevated urinary organic acids: phenylpropionylglycine, suberylglycine, hexanoylglycine, and medium chain dicarboxylic acids (C6>C8>C10);
- 3) molecular genetic studies confirming the presence of the 985 A>G mutation, or other less common mutations;
- 4) skin fibroblasts acylcarnitine probe assay demonstrating accumulation of characteristic acylcarnitines; or
- 5) skin fibroblasts enzyme studies showing reduced activity of MCAD.

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

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

## Results/discussion

In 2005, two cases of MCAD deficiency were confirmed in Canada. Both of the cases were detected through a newborn screening program, both diagnoses were confirmed by the presence of A985G mutation in homozygous form and both infants were asymptomatic.

**TABLE 16**

**Medium-chain acyl-coenzyme A dehydrogenase deficiency cases in 2006**

Reported	Duplicates	Excluded	Pending	Confirmed
15	0	0	6	9

In 2006, 15 cases of MCAD deficiency have been reported. Of these 15 cases, nine have been confirmed, five are pending confirmation and one has one mutation identified with further testing for a second mutation pending. Of the nine confirmed cases, seven were detected by newborn screening and two are siblings from one of the affected

infants that were detected as a result of a family study. Also, one of the nine confirmed cases had one common MCAD deficiency mutation (985 A>G) and one uncommon mutation for MCAD deficiency (250 C>T). Since the start of the study, all diagnosed patients have been asymptomatic and detected in provinces with newborn genetic screening programs in place.

## Conclusion

The MCAD deficiency study through the CPSP is a good means to identify cases and get data on all patients with MCAD deficiency on a timely basis. To enhance case ascertainment, this study is including representation from Canadian pathologists, particularly coroners. This is important since 25% of patients with MCAD deficiency unfortunately die at their first presentation. Metabolic laboratory directors are also participating in this study. Thus far, all identified patients were asymptomatic and detected through provincial newborn genetic screening programs, allowing for preventive measures, early treatment and better prognosis.

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# Non-type 1 diabetes mellitus

April 2006 to March 2008

## Highlights

- Obesity/overweight appears to be the single most important risk factor for T2DM.
- At diagnosis, 61% of children with T2DM had at least one obesity-related co-morbid condition.
- Medication-induced diabetes mellitus (MID) during childhood has been described with the use of glucocorticoids, chemotherapeutic agents and immunosuppressants.
- Children developing MID seemed to have different risk factors compared to children who develop T2DM.
- The realization that approximately 5% of children have monogenic diabetes rather than type 1 diabetes has resulted in the increased use of antibody testing at diagnosis.

## Background

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

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

recruited from the College of Family Physicians National Research System and endocrine registries, respectively, to maximize case ascertainment.

## Objectives

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

## Case definition

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

Clinical features suggestive of NT1DM include:

- Obesity (body mass index > 95<sup>th</sup> percentile for age and gender)
- Family history of T2DM in a first or second degree relative(s)
- Belonging to an ethnic group at high risk for non-type 1 diabetes (e.g., Aboriginal, African, Hispanic, South-Asian)
- A history of exposure to diabetes in utero (diagnosed before or during pregnancy)

- Acanthosis nigricans
- Polycystic ovarian syndrome
- Diabetes in a person with a syndrome often associated with type 2 diabetes (Prader-Willi Syndrome)
- Diabetes in a non-obese patient with at least one first degree relative and/or two second degree relatives with diabetes
- Minimal or no insulin requirement with a normal or near normal hemoglobin A1c level (4–6%) one year after diagnosis
- A diagnosis of diabetes while on medical therapy with a known diabetogenic medication (e.g., glucocorticoid, L-asparaginase, cyclosporine, tacrolimus, atypical antipsychotic, anticonvulsant)

#### Exclusion criteria

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

## Results

From April 1, 2006 to December 31, 2006 a total of 172 cases of NT1DM were reported. Of these, 161 cases were reported by paediatricians/paediatric endocrinologists, eight by family physicians, and three by adult endocrinologists. Sixteen cases were eliminated due to diagnosis of NT1DM outside the reporting period or failure to meet the criteria for diabetes as defined by the Canadian Diabetes Association (Table 17).

**TABLE 17**

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

Reported	Duplicates	Excluded	Pending	Confirmed
172	9	16	37	110

**TABLE 18**

**Classification of confirmed cases of  
non-type 1 diabetes mellitus**

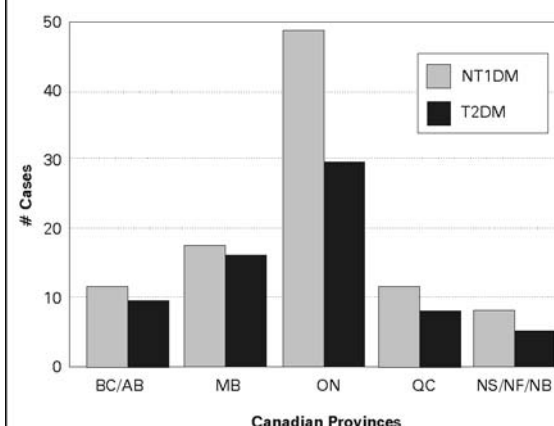
Confirmed	T2DM*	MID†	Monogenic DM	Indeterminate
110	71	20	8	11

\* Type 2 diabetes mellitus

† Medication-induced diabetes

**FIGURE 6**

**Provincial distribution of NT1DM and T2DM cases**



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

**TABLE 19**

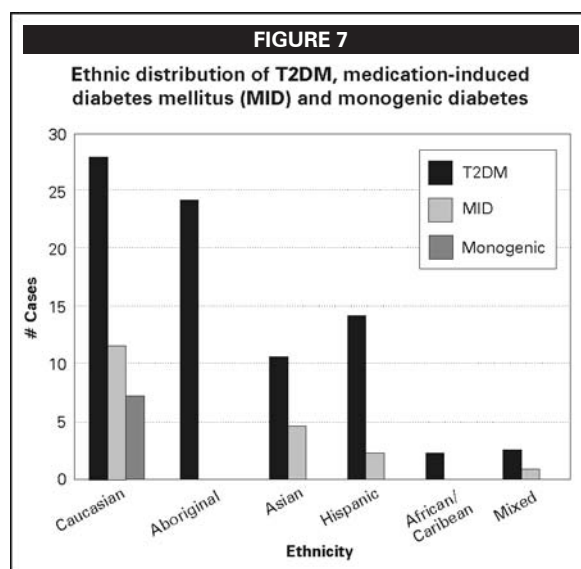
**Epidemiological and demographic data**

	T2DM (n=71)	MID (n=20)	Monogenic DM (n=8)
<b>Mean age (years)</b>	13.8	14.5	8.9
<b>Female : male ratio</b>	1.5:1	0.8:1	1:1
<b>Ethnicity (%)</b>			
Caucasian	28	60	100
Aboriginal	34	0	0
Asian	11	20	0
African/Caribbean	20	10	0
Hispanic	3	0	0
Mixed	4	5	0
Other	0	5	0
<b>Mean BMI</b>	32.6 (n=67)	24.4 (n=16)	18.9 (n=7)
<b>Mean BMI z-score</b>	2.1 (n=67)	0.7 (n=16)	0.9 (n=5)
<b>Positive family history* (%)</b>	81 (51/63)	44 (8/18)	86 (6/7)
<b>≥ 1 co-morbid condition at diagnosis (%)</b>	61 (41/67)	22 (4/18)	14 (1/7)
<b>Treatment (%)</b>			
Insulin	4 (3/70)	35 (7/20)	0
Oral hypoglycemics	1 (1/70)	0	13 (1/8)
Lifestyle counselling	30 (21/70)	25 (5/20)	75 (6/8)
Insulin and LC†	23 (16/70)	30 (6/20)	13 (1/8)
OH‡ and LC	26 (18/70)	0	0
Insulin, OH, and LC	16 (11/70)	0	0
No treatment	0	10 (2/20)	0

\* First or second degree relative with diabetes

† Lifestyle counselling

‡ Oral hypoglycemics



## Conclusion

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

Children with T2DM presented at a mean age of 13.8 years. Obesity/overweight appears to be the single most important risk factor for T2DM affecting nearly 100% of reported cases of clinically diagnosed T2DM. Of these cases, 13% presented with ketosis and 6% with ketoacidosis. The presence of ketosis may indicate a diagnosis of T1DM in an obese child. Close attention to the clinical course and measurement of pancreatic antibody levels may help clarify the diagnosis necessitating more readily available laboratory testing for pancreatic antibodies. Most children with T2DM have a positive family history of diabetes and many belong to high-risk ethnic groups; however, 28% of children with T2DM in this study were Caucasian. These findings stress

the importance of screening **all** obese adolescent and pre-adolescent children for diabetes as well as other features of the metabolic syndrome. Sixty-one percent (61%) of children diagnosed with T2DM had at least one obesity-related co-morbid condition **at diagnosis**. These preliminary data underscore the critical need for primary prevention programs targeted against childhood obesity that are essential in the prevention of T2DM and other obesity related co-morbidities.

The treatment of T2DM varies considerably depending on physician experience, physician bias, and local medical culture. In this study, 30% of patients with T2DM were treated with lifestyle counselling alone, whereas lifestyle counselling in combination with an oral hypoglycemic, insulin, and both an oral hypoglycemic and insulin occurred in 26%, 23% and 16% respectively. This reflects both the lack of a standardized approach to the treatment of childhood T2DM as well as the heterogeneity in presentation (e.g., asymptomatic to ketoacidosis). Study results will provide background data required to motivate the initiation of a national randomized control trial examining the efficacy and safety of various treatment modalities for T2DM in children and adolescents.

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

National surveillance for NT1DM in Canadian children will continue for a total of two years. This



study will be vital in providing epidemiological and demographic data on Canadian children affected with NT1DM, and specifically, obesity-related T2DM. These data will provide a foundation upon which specific paediatric health promotion and disease prevention programs can be established. This study also establishes a collaborative that will enable repeated estimates of NT1DM in the future. Therefore, this project will not only provide incidence rates of T2DM and other forms of NT1DM, but will also allow for future comparison of epidemiological data, recognition of national trends, and the assessment of the efficacy of health promotion and disease prevention programs. Furthermore, the Canadian incidence rate of NT1DM, and specifically, obesity-related T2DM, will be compared to other countries through collaboration with international surveillance units (e.g., the British Paediatric Surveillance Unit). Continued support from reporting physicians for the duration of this study is greatly appreciated by all investigators and collaborators.

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# Severe combined immunodeficiency

April 2004 to March 2008

## Highlights

- Three cases of SCID were confirmed in 2006.
- Two of the cases were referred for bone marrow transplant.
- One case has been reported thus far in an Aboriginal child.

## 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 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 are 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 recombinaise 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%).

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

## Objectives

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

## Case definition

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

- absolute lymphocyte count of less than 3,000/mm<sup>3</sup> or less than 20% CD3<sup>+</sup> T cells;
- familial history of primary immunodeficiency.

## Exclusion criteria

Exclude infants with HIV infection or cystic fibrosis.

## Results/discussion

There were three confirmed cases of SCID in 2006. Another five cases are pending, awaiting detailed case reports and/or further immunological data.

**TABLE 20**

**Severe combined immunodeficiency cases in 2006**

Reported	Duplicates	Excluded	Pending	Confirmed
9	1	0	5	3

Of the confirmed cases, two are males and one is female; all were born in Canada. One of the cases is an Aboriginal child. His BCG vaccine status was undetermined and he did not have any disseminated BCG infections. The average age at diagnosis is 5.8 months (range 3–12 months). Each of the confirmed cases had a different SCID type: X-linked, RAG-1 and ADA deficiency.

The main clinical features included persistent bronchiolitic-like illness and a rash. Two of the confirmed cases were referred for bone marrow transplant, but only one had received it by the time of reporting. All the cases were 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. With 15 confirmed cases in the first 32 months, the study is within the range of

expected numbers of new cases. Annual rates of SCID will be determined when all of the reported cases for a one-year period are diagnosed and analyzed. This study has been extended until March 2008, and may continue beyond that point if it is warranted.

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# Transfusion-related acute lung injury

September 2005 to August 2008

## Highlights

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

## Background

Transfusion of blood products can lead to various transfusion reactions. Transfusion-related acute lung injury (TRALI), although rare, is the leading cause of transfusion-related fatalities reported to the United States Food and Drug Administration (FDA). Patients develop acute lung injury rapidly, within six hours of initiating a transfusion of any blood product containing plasma (red blood cells, 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. Even though TRALI is becoming recognized more frequently in clinical practice and has received greater attention and description in the literature, it likely remains under-diagnosed and under-reported. This study would be the first one to assess incidence, presentation and the burden of TRALI in the paediatric population. The collection of national epidemiological data in the paediatric population will help to better describe the clinical presentation of TRALI, raise awareness and inform prevention strategies.

## Objectives

- 1) Determine the incidence of TRALI in the paediatric population using a standardized definition.
- 2) Describe the characteristics of patients and the clinical signs and symptoms associated with TRALI in the paediatric population.

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

## Case definition

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

### TRALI inclusion criteria (all three criteria must be present)

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

### TRALI exclusion criteria

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

### Possible TRALI

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

#### Direct lung injury

Aspiration  
Pneumonia  
Toxic inhalation  
Lung contusion  
Near drowning

#### Indirect lung injury

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

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

## Results

**TABLE 21**

**Transfusion-related acute lung injury cases in 2006**

Reported	Duplicates	Excluded	Pending	Confirmed
3	0	0	1	2

Two cases of TRALI were confirmed in 2006 and one case is pending a detailed questionnaire.

A seven-day-old infant underwent major cardiac surgery and received multiple transfusions during the operation. The TRALI occurred on post-operative day three, after administration of allogeneic red blood cells concentrate (20 cc/kg) over four hours. Within one hour after the end of the transfusion, the patient presented with dyspnea and desaturation (80%). The chest X-ray showed bilateral infiltrates. According to cardiac ultrasound and central venous pressure monitoring, the patient did not present cardiac dysfunction or circulatory overload. Oxygen therapy (35%) was provided and the patient gradually improved in the following 48 to 96 hours, without further complications.

A six-week-old infant with anemia of unknown origin and possible metabolic disease presented a TRALI after receiving a red blood cell concentrate (17 cc/kg) over four hours. Symptoms, which appeared three hours after the end of the transfusion, consisted of dyspnea, desaturation (88%), fever and tachycardia and were associated with a chest X-ray showing pulmonary edema. The patient received supplemental oxygen (1 L/minute) and diuretics and improved gradually over 24 to 48 hours, without further complications.

## Conclusion

More data will be required to interpret these results. As TRALI is a very rare phenomenon, it is not surprising that few cases have been reported thus far. A compounding factor is that TRALI presents as a clinical syndrome without a pathognomic confirmatory laboratory test; therefore, under-diagnosis and under-reporting are highly suspected. Other possible hypotheses for the rarity of cases include the following:

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

The continuation of the TRALI surveillance study will be important to help elucidate all these possibilities in the paediatric population. With more data, a comparative analysis could be performed using the capture-recapture method with TRALI cases reported through the Transfusion Transmitted Injuries Surveillance System (TTISS).

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

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# Survey Question

## Adverse events associated with paediatric complementary and alternative medicine

January 2006

Complementary and alternative medicine (CAM) is a broad umbrella term for a variety of practices (e.g., acupuncture, chiropractic, massage therapy) and natural health products (e.g., herbals, homeopathic remedies, vitamins). Recent surveys suggest that, although 20 to 50% of children use CAM, many families do not disclose use to their physicians. With CAM use so common among children, studies are needed to determine whether adverse events (AEs) are associated with paediatric CAM use.

The CPSP distributed the survey to 2,489 paediatricians in January 2006, to identify the frequency and severity of AEs associated with paediatric CAM. An AE was defined as any unfavourable or unintended sign (including abnormal laboratory finding), symptom or disease associated with the use of CAM. The survey asked three main questions: 1) how often do you ask patients about CAM use; 2) how many CAM-related AEs have you seen in the last year; and 3) have you seen a delayed diagnosis or treatment due to CAM use in a patient?

Of the 582 (23%) returned surveys, 38% of paediatricians stated that they ask patients

about their CAM use. Only 22% of respondents mentioned that patients disclosed CAM use before being questioned. Forty-two of the paediatricians (7%) said they had seen an AE associated with CAM use in the previous year, most commonly with natural health product use. In addition, 105 paediatricians reported 488 incidents of patients who had delayed diagnosis/treatment because of CAM use.

This study suggests that paediatric CAM-related AEs warrant further investigation. We suspect that our findings under-represent AEs related to paediatric CAM and support an active surveillance model to accurately assess incidence. The research team intends to partner with the CPSP to investigate serious AEs associated with paediatric CAM use. In 2007, an educational poster about CAM will be distributed by the CPS to improve communication about CAM use between families and paediatricians.

### Principal investigator

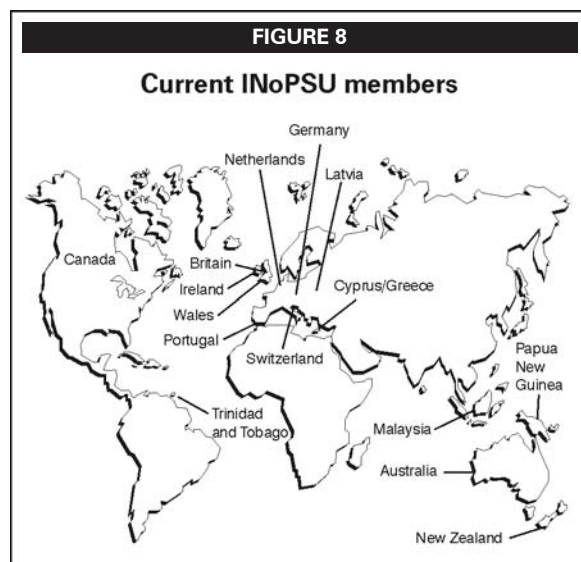
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# International Developments

## 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, Cyprus/Greece, Ireland, Latvia, Malaysia, Netherlands, New Zealand, Papua New Guinea, Portugal, Switzerland, Trinidad and Tobago, and Wales. The British Ophthalmological Surveillance Unit is an associate member.

The first formal INoPSU meeting was held in Ottawa, Canada in June 2000, with a second meeting taking place 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 and a fourth one was hosted by the British

Paediatric Surveillance Unit (BPSU) in London, England in the spring of 2006. The fifth INoPSU conference will take place in Munich, Germany in 2008.

Further information regarding all national paediatric surveillance units can be obtained on the INoPSU website at [www.inopsu.com](http://www.inopsu.com).

## Highlights from international collaboration

### BPSU 20<sup>th</sup> Anniversary Conference

The scientific program of the conference, held in May 2006, highlighted achievements of the BPSU over two decades of surveillance and celebrated the study results of two Sir Peter Tizard research bursaries: malaria in children and the incidence and characteristics of thyrotoxicosis in childhood.

### INoPSU 4<sup>th</sup> Conference

On May 31, 2006, the CPSP participated in the 4<sup>th</sup> INoPSU Conference with the following oral presentations: "International comparison of quality assurance criteria for acute flaccid paralysis surveillance," "International comparison of severe neonatal hyperbilirubinemia and herpes simplex virus infection" and "One-time surveys – CPSP added value." All of these presentations were very well received and stimulated interest and discussion.

### 47<sup>th</sup> Annual Meeting of the European Society for Paediatric Research (ESPR)

In October 2006, the CPSP also participated in the ESPR in Barcelona, Spain. A poster on "Neonatal diseases research through surveillance: The Canadian experience" was presented and many countries enquired about establishing active surveillance.

International collaboration of eight national surveillance units culminated in the publication of “Beyond counting cases – Public health impacts of national paediatric surveillance units” in the *Archives of Disease in Childhood* on December 11, 2006.

**TABLE 22**

**Studies under surveillance  
by national paediatric surveillance units in 2006**

Study	National Paediatric Surveillance Units
Acquired demyelinating syndromes of the central nervous system	CPSP
Acute encephalitis	PPSU
Acute flaccid paralysis	APSU, CPSP, NZPSU, SPSU
Acute rheumatic fever	SPSU, CPSP
Adolescent pregnancy	LPSU
Adverse drug reactions – serious and life threatening	CPSP
Ambiguous genitals	NSCK
Anorexia nervosa	NSCK
Cerebral palsy among five-year-olds	PPSU
Child abuse	NSCK
Child death review pilot	WPSU
Chronic interstitial lung disease	ESPED
Complications of measles	ESPED
Congenital cytomegalovirus infection	APSU, CPSP, PPSU
Congenital malformations from maternal anti-epileptic drug use	NSCK
Congenital myotonic dystrophy	CPSP
Congenital rubella syndrome	APSU, BPSU, NZPSU, SPSU, NSCK
Congenital toxoplasmosis	CGPSU
Diabetes mellitus	ESPED, NSCK
Down's syndrome	NSCK
Early-onset eating disorders	BPSU
Feto-maternal alloimmune thrombocytopenia (FMAIT)	BPSU
Hemolytic uremic syndrome	NZPSU, PPSU, SPSU, CGPSU
Head injuries secondary to suspected child maltreatment (abuse or neglect)	CPSP
Hemoglobinopathy	APSU, NSCK
Hepatitis C virus infection	APSU
Hereditary periodic fever syndrome	ESPED
HIV/AIDS	APSU, BPSU, NZPSU
Hodgkin's lymphoma	LPSU
Hyperinsulinemic hypoglycemia of infancy	APSU
Hyponatremia in infancy	WPSU
Inborn errors of metabolism	NZPSU
Influenza	ESPED
Ingestion of lamp oil (intoxications)	ESPED
Intussusception in childhood	ESPED, LPSU

Invasive <i>Haemophilus influenzae</i> infections (all types)	ESPED
Group B streptococcus sepsis	APSU, PPSU
Juvenile idiopathic arthritis	WPSU
Kawasaki disease	PPSU
Leukemia	LPSU
Malaria	BPSU
Medium-chain acyl-CoA dehydrogenase deficiency	NSCK, BPSU, CPSP
Methicillin resistant staphylococcus aureus (MRSA)	BPSU
Morbid obesity	NSCK
Nephrotic syndrome	NSCK, ESPED
Neonatal herpes simplex virus infection	APSU, SPSU, BPSU
Neonatal hyperbilirubinemia – severe	SPSU, NSCK
Neonatal sinus venous thrombosis	ESPED
Neural tube defects	SPSU
Neuroborreliosis	NSCK
Non-bacterial osteitis	ESPED
Non-cystic fibrosis bronchiectasis	IPSU
Non-Hodgkin's lymphoma	LPSU
Non-tuberculosis mycobacterial infection	APSU
Non-type 1 diabetes mellitus	CPSP, LPSU, WPSU
Peanut allergy	IPSU
Pertussis	SPSU
Pneumococcal sepsis/meningitis	ESPED, NZPSU
Progressive intellectual and neurological deterioration (PIND)	BPSU
Rett syndrome	APSU
Scleroderma	BPSU
Severe bronchiolitis requiring ICU care	IPSU
Severe combined immunodeficiency	CPSP
Severe retinopathy of prematurity	LPSU
Severe seatbelt injuries	APSU
Shaken baby syndrome	ESPED, SPSU
Stroke and transient ischemic attacks	IPSU
Systemic lupus erythematosus	ESPED
Transfusion-related acute lung injury	CPSP
Varicella (neonatal, congenital, and complications)	APSU, NSCK, PPSU
Vitamin D deficiency rickets	APSU, IPSU
Vitamin K deficiency bleeding/HDNB	APSU, BPSU, NZPSU, SPSU, NSCK

**Legend:**

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

## Highlights from other national paediatric surveillance units

### Australia

In 2006, the National Health and Medical Research Council of Australia awarded the Australian Paediatric Surveillance Unit (APSU) with a grant to develop a system for data collection among remote Aboriginal communities and migrant children. Preliminary results from the Vitamin D deficiency rickets study suggest the condition is more common in Australia than originally thought and predominantly affects the migrant community.

The APSU made three presentations at the biennial INoPSU conference in London: “Early-onset eating disorders in young children” (first report from the APSU and CPSP studies), “Fetal alcohol syndrome in Australia and New Zealand,” and “Beyond counting numbers: Public health impacts of national paediatric surveillance units,” which was also included in the *Archives of Disease in Childhood*. New studies in 2006 include: neonatal and congenital varicella and severe complications of varicella – coinciding with the recommendation for varicella vaccination in Australia, and severe seatbelt injuries – providing an opportunity to compare results with the CPSP study on lap-belt syndrome.

### Britain

To celebrate the completion of 20 years of surveillance, the BPSU held a conference in May for over 140 national and international attendees to showcase the work it has carried out. Robert Rodrigues Pereira from the Netherlands was appointed as the new INoPSU coordinator, while Alan Colver takes over as chair of the BPSU. New studies in 2006 include: malaria in childhood, vitamin K deficiency bleeding and feto-maternal alloimmune thrombocytopenia.

### Germany

The German Paediatric Surveillance unit (ESPED) was very active with 11 ongoing studies and three new ones (intussusception in childhood, shaken baby syndrome and non-bacterial osteitis). Kirsten Flügge et al. published, “Incidence and Clinical

Presentation of Invasive Neonatal Group B Streptococcal Infections in Germany,” in the journal *Pediatrics* (2006) 117:1139-45.

### Cyprus/Greece

The Cyprus/Greece Paediatric Surveillance Unit (CGPSU) focused on increasing public awareness of rare childhood infections and disorders. New studies in 2006 included: congenital toxoplasmosis to provide national incidence data and document laboratory testing methods prior to mandatory neonatal screening, and hemolytic uremic syndrome to assess the incidence of E. Coli O157:H7-HUS in children with regards to its occurrence in the animal population of the District of Thessaly and to ascertain the occurrence of other enteropathogens causing diarrhea-associated infections (such as *Salmonella*, *Shigella*, *Campylobacter*, *Yersinia*).

### Ireland

The Irish Paediatric Surveillance Unit (IPSU) continues active surveillance in the following areas: stroke and transient ischemic attacks, nutritional vitamin D deficiency rickets, severe bronchiolitis requiring ICU care, non-cystic fibrosis bronchiectasis and peanut allergy.

### Latvia

Among the highlights of the Latvian Paediatric Surveillance Unit (LPSU) in 2006 are the results of its study on leukemia, with eight cases reported as lymphoblastic and two cases as myeloblastic, as well as a study on lymphoma, with six cases of Hodgkin's and two cases of non-Hodgkin's. Additionally, in a study on adolescent pregnancy, the LPSU reported 481 cases of pregnant adolescents and 355 adolescents who underwent interruption of pregnancy. Concluding in 2006 are studies on severe retinopathy of prematurity and non-type 1 diabetes mellitus in children. The study on intussusception in early childhood is continuing.

### Netherlands

The Netherlands Paediatric Surveillance Unit's (NSCK) study on anorexia nervosa indicated an occurrence of 0.3%–0.6% in women aged 15–29 years. In the group of 15–19-year-olds, there appeared to be an increase from 79.6/million

women per year in 1987 to 109/million women per year in 1997. When excluding women older than 18 years, 296 cases were confirmed with an average age of 14.9 years and a female to male ratio of 10:1. These preliminary study results seem to indicate a higher incidence of anorexia nervosa than expected.

### **New Zealand**

The New Zealand Paediatric Surveillance Unit (NZPSU) presented four studies (shaken baby syndrome, hospitalization of infants with pertussis, infantile cholestasis and prevalence of HIV among pregnant women in New Zealand) at the 58<sup>th</sup> Annual Scientific Meeting of the Paediatric Society of New Zealand. Additionally, 2006 saw the publication of an article by Paul Heaton et al. entitled, "Kawasaki Disease in New Zealand," in the *Journal of Paediatrics and Child Health*.

### **Portugal**

The Portuguese Paediatric Surveillance Unit (PPSU) started four new studies in 2006: congenital cytomegalovirus infection, varicella zoster virus among hospitalized children and adolescents, epidemiology of Guillain-Barré

syndrome (GBS) infection until 90 days of life and cerebral palsy among five-year-olds. The PPSU actively participated in the INoPSU Conference and Business Meeting in London in May. The PPSU presented the final and partial results of all its studies since the unit's inception at the Portuguese Paediatric Congress in October. The final results of the GBS study were presented at the 14<sup>th</sup> European Workshop on Neonatology in Trondheim, Norway in September and at Europaediatrics in Barcelona, Spain in October.

### **Switzerland**

The Swiss Paediatric Surveillance Unit (SPSU) continues active surveillance on acute flaccid paralysis, congenital rubella syndrome, acute rheumatic fever, neural tube defects, neonatal herpes simplex, shaken baby syndrome, hemolytic uremic syndrome, vitamin K deficiency bleeding, pertussis and hyperbilirubinemia.

### **Wales**

The Welsh Paediatric Surveillance Unit (WPSU) continues active surveillance on juvenile idiopathic arthritis, hyponatremia, non-type 1 diabetes mellitus and a child death review pilot.



INoPSU Conference, London, May 2006

## 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

- 78% response from more than 2,400 paediatricians
- 87% data completion rate
- High duplicate reporting rate (17%) assuring case ascertainment and participant commitment

### Study ideas

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

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

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](mailto:cpssp@cps.ca)

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

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



**For more information on the  
Canadian Paediatric Surveillance Program  
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