



# CPSP

CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM



# 2008 RESULTS



Canadian  
Paediatric  
Society



Public Health  
Agency of Canada

Agence de la santé  
publique du Canada



## **Mission Statement**

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



# Enhanced surveillance in times of public health emergencies

## ② Situation in Canada

No sale of formula manufactured in China

Small risk remains in light of international travel, adoption and immigration

Recall from market of some products manufactured in China containing low levels of melamine

## ① Event in China

Mid-September 2008: Outbreak of renal stone disease; thousands hospitalized, some deaths associated with powdered infant formula contaminated with melamine

## ③ Action Plan

Emergency one-time survey, prepared in collaboration with the Public Health Agency of Canada and the New Zealand Paediatric Surveillance Unit, was sent within 10 working days to CPSP participants

## ④ Results

Response rate = 42%

Results available within three weeks

No cases associated with melamine-contaminated products

## ⑤ Lessons Learned

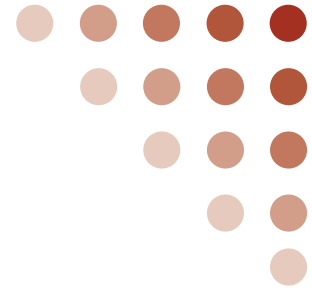
Collaborative partnerships effective in conducting enhanced surveillance of an emerging public health concern, quickly and inexpensively

Excellent added-value of an active national surveillance network, well connected with front-line paediatricians and public health officials



# Table of Contents

Acknowledgements .....	3
Foreword .....	4
Federal Minister of Health.....	4
Chief Public Health Officer of Canada .....	4
President of the Canadian Paediatric Society .....	5
CPSP Chairman .....	5
CPSP Steering Committee .....	6
CPSP Working Group .....	6
Publications 2004–2008.....	7
Published papers related to studies.....	7
Highlights published in 2008 in <i>Paediatrics &amp; Child Health</i> .....	8
Communication poster 2008 .....	8
Presentations in 2008 .....	9
National .....	9
International .....	10
Funding.....	11
Surveillance at Work.....	12
Overview .....	12
Investigators' corner.....	14
Studies timeline.....	15
Survey questions .....	15
CPSP Principal Investigators .....	16
Surveillance Studies in 2008.....	17
Completed:	
• Congenital cytomegalovirus infection (Final report) .....	17
• Head injury secondary to suspected child maltreatment (abuse or neglect) (Final report) .....	21
• Medium-chain acyl-coenzyme A dehydrogenase deficiency (Final report).....	24
• Non-type 1 diabetes mellitus (Final report) .....	26
• Transfusion-related acute lung injury (Final report) .....	30
Ongoing:	
• Acute flaccid paralysis.....	33
• Adverse drug reactions – serious and life-threatening .....	37
• Bulimic eating disorders .....	40
• Congenital myotonic dystrophy .....	42
• Juvenile idiopathic arthritis.....	44
• Kernicterus .....	47
• Methicillin-resistant <i>Staphylococcus aureus</i> in hospitalized children .....	50
• Severe combined immunodeficiency .....	52
Survey Questions .....	54
Assessing CPSP surveillance methodology for ADR reporting .....	54
Paediatric pre-travel care .....	55
Renal stones and/or unexplained acute renal failure in infants .....	55
Travel-related illnesses in paediatrics .....	56
International Developments.....	57
Highlights from international collaboration.....	57
Highlights from other national paediatric surveillance units.....	59
Research Opportunities – Call for New Studies .....	inside back cover



# Acknowledgements

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

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 11 in this report.

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

# Foreword

## Federal Minister of Health

The health of Canadian children and youth is critical to this country's future. For the last thirteen years, the Canadian Paediatric Surveillance Program has made an important contribution to this aspect of our health system by helping monitor diseases and conditions in Canada's young people. The program has led to a greater awareness of those diseases that affect our children and youth, and provided a better understanding of risk factors.

The Government of Canada is committed to improving the health of young Canadians. In addition to supporting this program, \$80 million was committed by the Canadian Institutes of Health Research in 2008 to research related to child health and early childhood development. The Government is also currently providing \$105.4 million a year for Aboriginal children and youth health programs through Health Canada's First Nations and Inuit Health Branch.

I congratulate members of the Canadian Paediatric Society on another successful year implementing the Surveillance Program and on the completion of the program's 13<sup>th</sup> annual report.

On a broader note, your dedication to and caring for young people and their families are highly valued by all Canadians.

We look forward to continuing our work with the Canadian Paediatric Society, its members, the provinces and territories, and other partners to provide Canadian children and youth with a healthier future.



The Honourable  
Leona Aglukkaq

## Chief Public Health Officer of Canada

I am delighted to introduce the 13<sup>th</sup> annual report of the Canadian Paediatric Surveillance Program (CPSP), an important collaboration of the Canadian Paediatric Society (CPS) and the Public Health Agency of Canada.

This year, the CPSP demonstrated that it could be mobilized quickly to conduct enhanced surveillance in the event of an emerging public health concern in children. The outbreak of renal stones and renal failure in very young children in China, associated with consumption of milk formula contaminated with melamine, raised the question of whether children in Canada were being similarly affected. When the CPSP participants were surveyed regarding this issue, their rapid response gave us the needed information.

I would like to thank the paediatricians who take the time to contribute to this program every month. Without their support, this program would not exist.

I would also like to acknowledge the work of the CPSP Steering Committee, the CPS staff, and the Public Health Agency of Canada staff who contribute to the ongoing success of the program.

Congratulations and thank you for your continued efforts.



Dr. David  
Butler-Jones

# President of the Canadian Paediatric Society

As President of the Canadian Paediatric Society, I am proud that we have such a well-established and active surveillance system in Canada to monitor and increase awareness of rare diseases in children and youth.

During my time on the CPS Board of Directors, and as past chair of the CPS Infectious Diseases and Immunization Committee, I have seen first-hand how surveillance study results can have tangible and lasting impacts that change the way that practitioners care for children and youth, and the government laws that affect their well-being and safety.

Over the years, studies on vaccine-preventable diseases have shown the success of immunization programs as well as confirmed the need for the development of new vaccines. Clinical practice guidelines and health planning services have also seen important changes, and injury prevention surveillance has clearly identified products that pose serious health hazards.

A program like the CPSP would not be successful without the dutiful reporting each month from all paediatricians and paediatric subspecialists in Canada. Thank you all for your important contribution to this research.



Dr. Joanne Embree

## CPSP Chairman

It is an exciting time to chair the CPSP. Health Canada has renewed its commitment and support, and CPSP studies continue to break new ground, addressing paediatric health issues of great importance to Canadian families, health providers and policy makers. Over the past year, the CPSP demonstrated its ability to rapidly respond to an emergent public health concern related to melamine. CPSP studies on high-impact conditions, such as kernicterus and non-type 1 diabetes mellitus, also continue to influence public health policy and paediatric practice.

My goals during my term as chair are to:

- Maintain the quality and momentum of the program
- Work with potential investigators to extend national surveillance to other priority conditions that affect Canadian children
- Pilot-test Web-based reporting as an evolving surveillance methodology
- Work collaboratively with the steering committee to address surveillance gaps, such as acquiring data from children living in rural and remote communities, including Aboriginal children
- Support strong collaboration with other members of the International Network of Paediatric Surveillance Units



Dr. Lonnie Zwaigenbaum

Thanks to all participants and contributors. In particular, we are indebted to paediatricians and paediatric subspecialists for completing the monthly surveillance forms and case reports, which provide the foundation for all the important work of the CPSP. I am looking forward to many more productive years of national epidemiological research.

# CPSP Steering Committee

Dr. Lonnie Zwaigenbaum (Chair)	Canadian Paediatric Society
Dr. Laura Arbour*	Canadian College of Medical Geneticists (Liaison)
Dr. Garth Bruce*	Canadian Paediatric Society
Dr. Denis Daneman	Paediatric Chairs of Canada
Ms. Marie Adèle Davis	Canadian Paediatric Society
Dr. Kimberly Dow	Paediatric Chairs of Canada / Canadian Paediatric Society
Dr. Kevin Gordon	Canadian Association of Child Neurology (Liaison)
Dr. Danielle Grenier	Canadian Paediatric Society
Dr. W. James King	Canadian Paediatric Society
Ms. Melanie Laffin Thibodeau	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	Canadian Paediatric Society
Dr. Lesley Ann Turner	Canadian College of Medical Geneticists (Liaison)
Ms. Anne-Marie Ugnat	Centre for Health Promotion, Public Health Agency of Canada
Dr. Wendy Vaudry	IMPACT (Immunization Monitoring Program ACTIVE) (Liaison)
Dr. Lynne Warda*	Canadian Paediatric Society
Dr. Sandra Woods	Canadian Paediatric Society

\* Our sincere thanks to members who completed their terms in 2008 for their work on the CPSP Steering Committee.

# CPSP Working Group

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

The CPSP wishes to thank Louise Painchaud for her dedicated commitment as Senior Coordinator for the past two years.



# Publications 2004-2008

## Published papers related to studies

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

### Acute flaccid paralysis

AFP surveillance in Canada. Macey J, Lipskie T. *Pan American Health Organization Immunization Newsletter*, Apr 2007; XXIX(2): 1-3

### Cerebral edema

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

### CHARGE syndrome

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

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

### Child maltreatment

The Canadian Paediatric Surveillance Program: A framework for the timely data collection on head injury secondary to child maltreatment. Bennett S, Grenier D, Medaglia A. *Am J Prev Med* 2008;34(4S):S140-2

### Haemolytic uraemic syndrome

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

### Hemorrhagic disease of the newborn

Canadian Paediatric Surveillance Program confirms low incidence of hemorrhagic disease of

the newborn in Canada. McMillan DD, Grenier D, Medaglia A. *Paediatr Child Health* 2004;9(4):235-8

### Kernicterus / neonatal hyperbilirubinemia

Prevention of kernicterus – New guidelines and the critical role of family physicians. Shaw E, Grenier D. FP Watch, *Can Fam Physician* 2008;54(4):575-6

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

### Lab-belt syndrome

The spectrum of seat belt syndrome among Canadian children: Results of a two-year population surveillance. Santschi M, Lemoine C, Cyr C. *Paediatr Child Health* 2008;13(4):279-83

### Necrotizing fasciitis

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

### Neonatal herpes simplex virus infections

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

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

### Progressive intellectual and neurological deterioration

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

### Smith-Lemli-Opitz syndrome

Incidence of Smith-Lemli-Opitz syndrome in Canada: Results of three-year population surveillance.

Nowaczyk MJM, Waye JS, Zeesman S, Douketis JD. *J Pediatr* 2004;145(4):530-5

### **Subacute sclerosing panencephalitis**

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

### **Surveillance – General**

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

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

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

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

### **Vitamin D deficiency rickets**

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

## **Highlights published in 2008 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* 2008;13(10): 842, 849, 856

Bulimia: A secretive turmoil. *Paediatr Child Health* 2008;13(9):772

Unravelling a failed newborn hearing screening. *Paediatr Child Health* 2008;13(8):723

Surviving an adverse drug reaction. *Paediatr Child Health* 2008;13(7):610

Complementary and alternative medicine in paediatrics: Looking at the safety profile. *Paediatr Child Health* 2008;13(6):492

Severe combined immunodeficiency: A tale of two brothers. *Paediatr Child Health* 2008;13(5):386

Newborn jaundice: Time for prevention? *Paediatr Child Health* 2008;13(4):298

Challenge for timely diagnosis of juvenile idiopathic arthritis in children. *Paediatr Child Health* 2008;13(3):192

Magnets in the bowel: A sticky problem! *Paediatr Child Health* 2008;13(2):118

Rickets: A re-emerging public health problem in Canada? *Paediatr Child Health* 2008;13(1):73

## **Communication poster 2008**



# Presentations in 2008

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

## National

### Acute flaccid paralysis

Ensuring our polio-free status: active acute flaccid paralysis surveillance (AFP) in Canada. Garner MJ, Macey JF, Desai S, Grenier D. Canadian Immunization Conference, Toronto, in December. (Poster)

### Adverse drug reactions

The power of adverse drug reaction reporting. Zimmerman M, Rieder M. Canadian Paediatric Society Annual Conference, Victoria, in June. (Oral)

### Child maltreatment

The extent and nature of head injury secondary to child maltreatment in Canada: A 3-year surveillance study. Bennett S, Fortin G, Ward M. Seventh North American Conference on Shaken Baby Syndrome/Abusive Head Trauma, Vancouver, in October. (Oral)

### Congenital cytomegalovirus infection

Congenital cytomegalovirus infection in Canada: Cases reported by pediatricians to the Canadian Paediatric Surveillance Program, Vaudry W, Lee BE, Rosychuk R, Pelletier L. Canadian Paediatric Society Annual Conference, Victoria, in June. (Oral)

### Kernicterus / neonatal hyperbilirubinemia

The incidence of kernicterus in Canada 2007–2009. Sgro M, Campbell D, Shah V. Canadian Paediatric Society Annual Conference, Victoria, in June. (Oral)

Severe neonatal hyperbilirubinemia and neurological findings in Canada. Sgro M, Campbell D, Barozzino T, Fallah S, Shah V. Canadian Paediatric Society Annual Conference, Victoria, in June. (Oral)

The incidence of kernicterus in Canada. Sgro M. 7<sup>th</sup> Annual Neonatal & Maternal-Fetal Medicine Research Day. Mount Sinai Hospital, Toronto, in April. (Invited lecture)

### Magnet ingestions

Multiple magnet ingestions in Canadian children: A survey of Canadian health care providers. D'Mello JR, Warda L, Briggs G. Canadian Paediatric Society Annual Conference, Victoria, in June. (Poster)

### Medium chain acyl-coenzyme A dehydrogenase deficiency

Incidence of medium chain acyl-coenzyme A dehydrogenase deficiency in Canada using the Canadian Paediatric Surveillance Program (September 2005 – September 2008). Prasad C, Speechley KN, Dyack S, Rupar CA, Chakraborty P, Kronick JB. Canadian College of Medical Geneticists Annual Scientific Meeting, St. John's, in September. (Poster)

### Non-type 1 diabetes

Sentinel network collaboration for pan-Canadian surveillance of NT1DM. Hamilton J, Dean H, Amed S, Lambert-Lanning A, Laubscher T, Dannenbaum D. Family Medicine Forum, Toronto, in November. (Oral)

National surveillance for non-type 1 diabetes (NT1DM) in Canadian children. Amed S, Dean H, Hamilton J, NT1DM Study Team. CDA/CSEM Professional Conference and Annual Meetings, Montreal, in October. (Oral)

### Surveillance – General

Injury prevention surveillance: A research asset for advocacy. Grenier D, Davis MA, Ugnat A-M, Laffin Thibodeau M. Family Medicine Forum, Toronto, in November. (Poster)

Indigenous health research through surveillance. Grenier D, Ugnat A-M, Painchaud L. Canadian Paediatric Society Annual Conference, Victoria, in June. (Poster)

## International

### **Congenital myotonic dystrophy**

Medical morbidity and mortality in a population-based sample of congenital myotonic dystrophy. Ho A, Campbell C. Muscle Study Group Meeting, Buffalo, in September. (Poster)

### **Eating disorders**

Restrictive eating disorders in children: Global findings from the International Network of Paediatric Surveillance Units. Pinhas L. International Conference on Eating Disorders, Seattle, in May. (Oral)

### **INoPSU**

Impacts of the International Network of Paediatric Surveillance Units. Grenier D. Annual Conference of the German Pediatric Society and the 5<sup>th</sup> INoPSU Meeting, Munich, in September. (Oral)

Impacts of the International Network of Paediatric Surveillance Units. Grenier D. The Royal Australasian Paediatric Congress, Adelaide, in May. (Oral)

### **Juvenile idiopathic arthritis**

Canadian national surveillance for juvenile idiopathic arthritis. Tucker LB, Dancey P, Oen K, Huber A, Lagacé C, Espinosa V, and the Canadian Alliance for Pediatric Rheumatology Investigators (CAPRI). American College of Rheumatology Annual Scientific Meeting, San Francisco, in October. (Oral)

### **Kernicterus / neonatal hyperbilirubinemia**

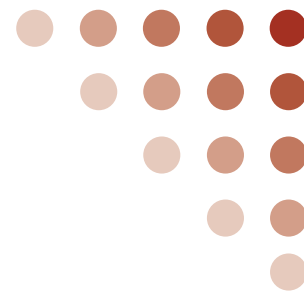
The incidence of kernicterus in Canada 2007–2009. Sgro M, Campbell D, Shah V. Pediatric Academic Societies (PAS) Annual Meeting, Honolulu, in May. (Poster)

Severe neonatal hyperbilirubinemia and neurological findings in Canada. Sgro M, Campbell D, Barozzino T, Fallah S, Shah V. Pediatric Academic Societies (PAS) Annual Meeting, Honolulu, in May. (Poster)

### **Rheumatic fever**

Rheumatic fever in Canada: Results from a national surveillance program. Dancey P, Templeton C, Human DG, Rahman P, Cooper A. American College of Rheumatology, Pediatric Rheumatology Symposium, Keystone, in March. (Poster)

# 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.

The CPSP is a collaborative program of the Canadian Paediatric Society and the Public Health Agency of Canada, with financial support from Health Canada's Therapeutic Effectiveness and Policy Bureau.

We gratefully acknowledge the following organizations that have provided funding to the CPSP during part or all of 2008.

## Non-governmental sources

- Canadian Medical Protective Association
- Children's Health Research Institute (Children's Hospital of Western Ontario)
- Children's Hospital of Eastern Ontario
- Children's Optimal Therapeutics Program, Children's Health Research Institute
- Division of Endocrinology, The Hospital for Sick Children
- Garrod Association
- Héma-Québec
- IWK Health Centre – Dalhousie University
- Lawson Health Research Institute
- Psychiatry Endowment Fund, The Hospital for Sick Children
- University of Manitoba
- William Singeris National Centre for Myotonic Dystrophy Research

# Surveillance at Work

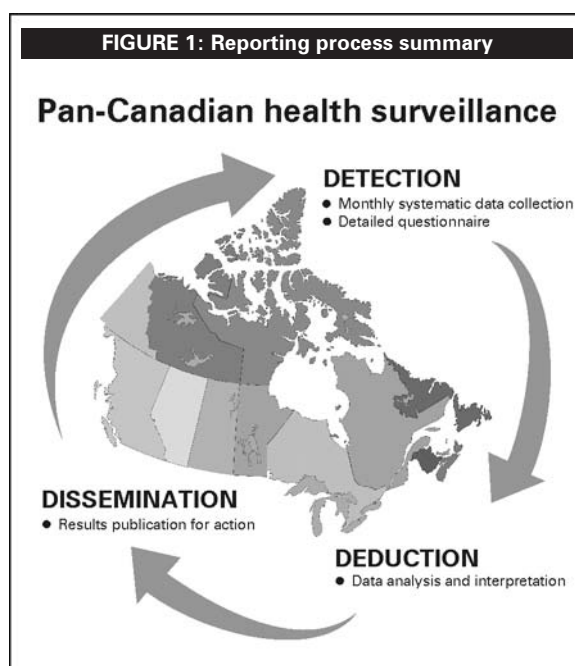
## Overview

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

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

## Process

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



## Reporting

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

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

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



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

**TABLE 1**

**Initial response rates (%)  
and number of participants for 2008**

Provinces/territories	Reporting rates (%)	Number of participants
Alberta (AB)	79	300
British Columbia (BC)	77	275
Manitoba (MB)	77	120
New Brunswick (NB)	80	30
Newfoundland and Labrador (NL)	87	51
Nova Scotia (NS)	86	100
Northwest Territories (NT)	100	3
Nunavut (NU)	100	1
Ontario (ON)	80	991
Prince Edward Island (PE)	87	7
Quebec (QC)	77	660
Saskatchewan (SK)	67	57
Yukon (YT)	100	2
<b>Canada</b>	<b>80</b>	<b>2,597</b>

**TABLE 2**

**2008 detailed questionnaire completion rates  
as of May 1, 2009**

Studies/conditions	Reported cases*	Pending	% Completion rate
Acute flaccid paralysis	39	2	95
Adverse drug reactions – serious and life-threatening	63	13	79
Bulimic eating disorders	109	12	89
Congenital cytomegalovirus infection	2	1	50
Congenital myotonic dystrophy	3	0	100
Head injury secondary to suspected child maltreatment (abuse or neglect)	11	2	82
Juvenile idiopathic arthritis	371	1	99
Kernicterus	8	1	88
Medium-chain acyl-coenzyme A dehydrogenase deficiency	17	1	94
Methicillin-resistant <i>Staphylococcus aureus</i> in hospitalized children	46	7	86
Non-type 1 diabetes mellitus	44	0	100
Severe combined immunodeficiency	4	1	75
Transfusion-related acute lung injury	1	0	100
<b>Total number of cases (all studies)</b>	<b>718</b>	<b>41</b>	<b>94</b>

\* Excluding duplicate and excluded cases

Participants who do not reply every month receive quarterly reminders. In addition, information on the monthly compliance rates and the number of cases reported is mailed quarterly to all participants to keep

them informed of progress. The CPSP is encouraged by the 80% national reporting rate (Table 1) and the 94% response rate for completion of detailed questionnaires (see Table 2 for study breakdown).

## Participant workload

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

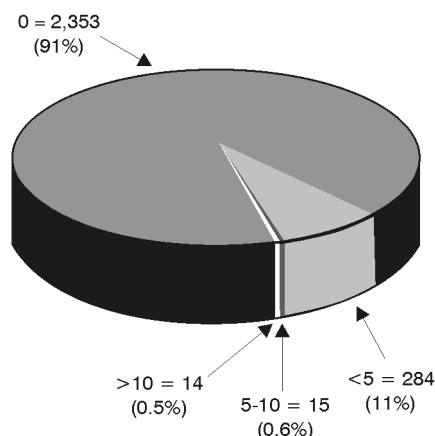
In 2008, the majority of participants (91%) had 'nil' cases to report. The importance of zero reporting must be re-emphasized. Figure 2 illustrates the number of cases reported by respondents in 2008. As studies come and go, the workload shifts to different subspecialties. The 2008 studies with the most reports were Juvenile idiopathic arthritis and Bulimic eating disorders.

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,

**FIGURE 2**

**Number of cases reported  
by respondents in 2008**



letters of appreciation were sent to participants who completed the initial reporting forms for all months in 2008 and/or returned one or more detailed questionnaires. In addition, Drs. Roger Gough Nicholson (Ontario) and Richard S. Taylor (Alberta) were selected in this year's early-bird draw, each winning a copy of the Canadian Paediatric Society publication *Well Beings: A guide to health in child care*. The lucky winners of the year-end draws for complimentary registration for the June 2008 CPS Annual Conference in Ottawa, Ontario, were Dr. Amuchou S. Soraisham (Alberta), who responded for all months in 2008, and Dr. Margaret Gan-Gaisano (Ontario), 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 2,597 participants. The program is committed to a case ascertainment rate of over 90% and, due to follow-up reminders to non-respondents, obtains a response rate of 94% 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 those that could not be undertaken any other way. Following the review, studies must receive ethical approval and have external funding arrangements in place before final acceptance to the program. Researchers interested in obtaining more information about the program are encouraged to visit the website at [www.cps.ca/cpsp](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 2008 one-time survey questions are found on pages 54-6.

**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)

Study	Start date	End date	Total confirmed cases to December 31, 2008
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	104
CHARGE association/syndrome	September 2001	August 2004	90
Congenital rubella syndrome	January 1996	December 2004	9
Prader-Willi syndrome	January 2003	December 2004	31
Early-onset eating disorders	March 2003	February 2005	160
Lap-belt syndrome	September 2003	August 2005	28
Osteogenesis imperfecta	January 2004	December 2005	27
Acquired demyelinating syndromes of the central nervous system	April 2004	March 2007	221
Acute rheumatic fever	April 2004	March 2007	68
Congenital cytomegalovirus infection	March 2005	February 2008	49
Head injury secondary to suspected child maltreatment (abuse or neglect)	March 2005	February 2008	220
Non-type 1 diabetes mellitus	April 2006	March 2008	319
Medium-chain acyl-coenzyme A dehydrogenase deficiency	September 2005	August 2008	46
Transfusion-related acute lung injury	September 2005	August 2008	4
Juvenile idiopathic arthritis	October 2007	September 2009	471
Adverse drug reactions – serious and life-threatening	January 2004	December 2009	192
Kernicterus	January 2007	December 2009	2
Congenital myotonic dystrophy	March 2005	February 2010	23
Bulimic eating disorders	March 2008	February 2010	77
Severe combined immunodeficiency	April 2004	March 2010	23
Methicillin-resistant Staphylococcus aureus in hospitalized children	September 2008	August 2010	29
Acute flaccid paralysis	January 1996	December 2010	562

## Survey questions

TABLE 6

CPSP survey questions

Injuries associated with baby walkers	January 2002
Lap-belt syndrome	February 2003
Acquired demyelinating syndromes of the central nervous system (CNS)	February 2004
Infant bath seats	June 2004
Acute flaccid paralysis	November 2004
Congenital cytomegalovirus infection	January 2005
International adoption	September 2005
Adolescent depression and side effects of selective serotonin reuptake inhibitors (SSRI)	November 2005
Adverse events associated with paediatric complementary and alternative medicine	January 2006
Magnetic toys	August 2007
Assessing CPSP surveillance methodology for ADR reporting	January 2008
Paediatric pre-travel care	February 2008
Travel-related illnesses in paediatrics	August 2008
Renal stones and/or unexplained acute renal failure in infants	October 2008

# CPSP Principal Investigators



## Surveillance studies in 2008



Dr. Wendy Vaudry  
Congenital  
cytomegalovirus  
infection



Dr. Susan Bennett  
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. France Gauvin  
Transfusion-related  
acute lung injury



photo not  
available at time  
of publication  
  
Dr. Shalini Desai  
Acute flaccid paralysis



Margaret Zimmerman  
Adverse drug  
reactions – serious  
and life-threatening



Dr. Leora Pinhas  
Bulimic eating  
disorders



Dr. Craig Campbell  
Congenital myotonic  
dystrophy



Dr. Lori Tucker  
Juvenile idiopathic  
arthritis



Dr. Michael Sgro  
Kernicterus



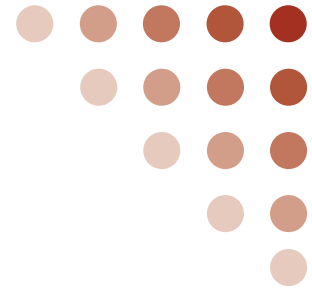
Dr. Nicole Le Saux  
Methicillin-resistant  
*Staphylococcus aureus*  
in hospitalized children



Dr. RoseMarie Ramsingh  
Severe combined  
immunodeficiency



# Surveillance Studies in 2008



## Congenital cytomegalovirus infection

March 2005 to February 2008 – Final report

### Highlights

- The study identified 49 cases of confirmed cCMV infection, representing 0.54 cases per 10,000 births. This is just over 10% of the expected number of cases.
- Impaired growth is the commonest clinical presentation, and thrombocytopenia is the commonest laboratory abnormality.
- Paediatricians are detecting severely affected infants in the prenatal or neonatal period; of note, only half of infants with neurological disease are being treated with antiviral therapy.
- New Canadian, First Nations, and rural children appear to be at higher risk.
- To optimize outcomes for infants with cCMV, routine screening may need to be considered as a public health policy.

### Background

Congenital cytomegalovirus infection (cCMV) is the most common congenital infection, affecting from 0.2% to 2.4% of all live births, but Canadian data are scarce. Approximately 10% of infected infants manifest significant clinical illness in the newborn period. While almost all of these symptomatic newborns will have neurologic sequelae, so will another 5–17% of asymptomatic newborns. cCMV infection is the commonest cause of nonhereditary deafness in children and may be progressive over years. This infection is a difficult diagnosis to prove retrospectively, as virus must be identified from the newborn in the first three weeks of life; virus isolation beyond that age may indicate acquired infection.

Active surveillance is timely for several reasons. Universal newborn hearing screening is being recommended and implemented; however, progressive hearing loss from cCMV infection will be missed. Ganciclovir therapy in neonates with neurological manifestations improves hearing outcome. CMV vaccines are currently being developed.

### Objectives

- 1) Determine the number of cCMV 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<sup>\*</sup>
- Polymerase chain reaction (PCR) positive for CMV from an appropriate clinical specimen
- Presence of CMV-specific IgM in the neonatal or cord blood<sup>†</sup>

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

<sup>†</sup> 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

**TABLE 7**

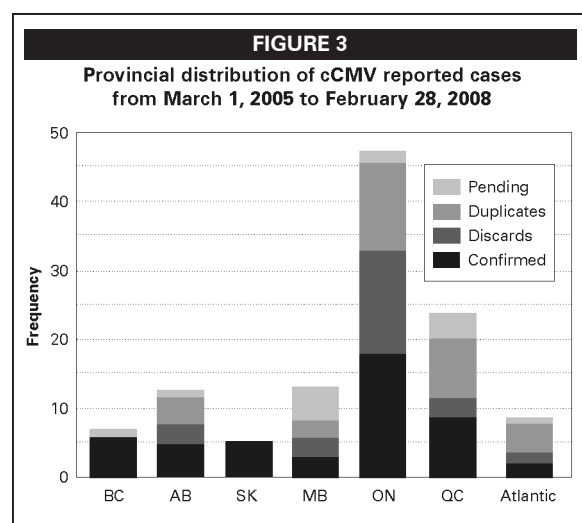
**Congenital cytomegalovirus infection cases  
from March 1, 2005 to February 28, 2008**

Year	Reported	Duplicates	Excluded	Pending	Confirmed
2005*	39	13	6	1	19
2006	43	10	8	6	19
2007	34	8	13	2	11
2008†	2	0	1	1	0
<b>Total</b>	<b>118</b>	<b>31</b>	<b>28</b>	<b>10</b>	<b>49</b>

\* March 1 to December 31, 2005

† January 1 to February 28, 2008

There have been 49 cCMV confirmed cases to date. Table 7 summarizes the status of the 118 reported cases and Figure 3 summarizes the provincial distribution.



### Cumulative results from March 2005 to February 2008

#### Demographic and epidemiologic data

Six of the confirmed cases (12%) were from rural areas (population <1,000) and four of these rural cases were born to First Nations women. Thirty-five (71%) of the mothers were born in Canada, six (12%) were born outside the country and eight had an unknown country of birth. Data on employment history, educational status and daycare exposure were collected but no significant trends were demonstrated. Ethnic origin was reported for 40 (82%) of the mothers; 22 (45%) were Caucasian

and eight (16%) were Aboriginal. The median age of the mothers was 23 years (range 17–41) and 21 (43%) mothers were primigravida.

#### Clinical presentation

Twenty-eight (57%) of the congenitally infected infants presented prenatally: three by maternal serology, indicating primary infection, and 25 by fetal imaging showing either intrauterine growth restriction (IUGR) or cranial abnormalities. The rest of the infants first presented in the neonatal period and were investigated because of symptoms. A summary of the characteristics of all diagnosed infants follows.

Thirty-two (65%) of the infants were male. The median birth weight was 2,165 grams (range 1,055–3,678), median length was 46 centimetres (range 33–53) and median head circumference was 31 centimetres (range 26–38). The median gestational age was 36 weeks (range 26–41). Twenty-three (47%) infants were small for gestational age and 18 (37%) were reported to have microcephaly. Fewer than 25% of the infants were reported to have hepatomegaly, splenomegaly or rash. Fifteen (31%) had congenital anomalies. The most common laboratory abnormality was thrombocytopenia reported in 26 (53%) cases, which was more than twice as common as any one of anemia, hyperbilirubinemia or hepatitis.

To be included as a case, CMV diagnostic testing had to be completed before three weeks of age. Diagnostic testing performed after this age was the most common reason for excluding a reported case. A variety of diagnostic tests were sent from reporting centres. Urine viral isolation or PCR was positive in 100% of cases. Neonatal IgM to CMV was done in only 21 (43%) cases and was positive in 10 for a sensitivity of 48%. PCR on the blood was positive 3/8 (38%) times that it was performed and CSF PCR was positive 0/13 (0%) times it was performed.

#### Management and burden of illness

Most of the infants had some form of cranial imaging including head ultrasounds, cranial MRI or CT scans. Hearing assessments had been completed on most infants with some reports indicating that

hearing assessments were planned but had not yet been completed. Administration of antiviral therapy with ganciclovir intravenously was reported for 13 (27%) of the infants. All of these infants had significant neurological disease. However, half (18/36) of the infants who were not treated also had significant neurological disease.

The infected infants remained in the reporting hospital for a combined total of more than 1,294 days; 712 of these were intensive care unit (ICU) days. These are minimum estimates as paediatricians sometimes reported only the length of stay at their hospital, before the infant was transferred to a tertiary care centre. Median length of stay reported was 25 days with a median of 10 days in the ICU. There was a total of four deaths. The rest of the infants were discharged home or transferred to another facility during the reporting period and the final outcomes are not known.

## Discussion

New Canadian, First Nations, and rural children appear to be at higher risk of congenital CMV infection; 67% of the infected children born in rural Canada were of First Nations origin. No other demographic risk factors were detected. The most common clinical presentation was growth impairment with almost half of infants reported as small for gestational age and over one-third being microcephalic. Other commonly expected signs of congenital infection such as hepatomegaly, splenomegaly, rash and jaundice were reported in a smaller proportion of cases. Thrombocytopenia was the commonest laboratory abnormality. Congenital CMV caused significant morbidity during the neonatal reporting period, with affected infants experiencing prolonged hospital stays of high intensity. The long-term morbidity was not assessed with this study. Four infants died, for an early mortality rate of 8%.

Viral isolation, or PCR, confirmed the diagnosis from the urine in all cases. Neonatal IgM to CMV was performed in a minority of cases and had a low sensitivity. The low rate of serological testing may be a result of the pre-study survey and educational intervention with CPSP participants. Antiviral therapy with intravenous ganciclovir

was administered in 27% of the infants all of whom had neurological disease. Although there is evidence that infants with neurological involvement benefit from antiviral therapy in the newborn period, half of the infants who did not receive antiviral therapy also had neurological involvement.

The surveillance study has identified 49 cases of confirmed cCMV. According to the last published Canadian data, the rate of cCMV infection identified was 0.4%. This would lead us to expect four symptomatic infections per 10,000 births. Assuming a Canadian birth cohort of 300,000 per year, this study identified 0.54 per 10,000 births. This is just over 10% of the expected number. This suggests that either the infection rate is much lower in Canada, or that cases are not being diagnosed or reported by paediatricians. Although some cases may not be reported, the high response rate and history of cooperation from participants suggest that under-reporting would not account for 90% of unreported cases. Therefore, the most likely explanation remains underdiagnosis. This observation is also reinforced by the severity of confirmed cases and the proportion of those diagnosed antenatally because of the severity of changes on the ultrasound. In fact, more cases were initially suspected by obstetricians than by paediatricians. Many symptomatic infants are likely being missed by clinicians because of a milder spectrum of disease presentation. These cases may be more subtle in the neonatal period and either not ever recognized as cCMV or not tested early enough in the neonatal period to make a definitive diagnosis. Undiagnosed infants will not be considered for antiviral therapy or early intervention and follow-up for hearing or developmental outcomes.

The most accurate measurement of the cCMV infection rate will likely have to await population-based surveillance to capture the full spectrum of the infection as previous studies have suggested a much higher rate of symptomatic cases than identified by this surveillance. This study strongly suggests that only those infants severely affected are currently diagnosed. Clearly, many infants are not identified when relying solely on clinical

diagnosis. Comparisons of infection rates detected by the CPSP and population-based screening are important to assess the need for implementation of universal routine screening for cCMV. This gap is an important public health priority to be addressed.

## Conclusion

At present only severely affected infants with cCMV in the prenatal or neonatal period are being recognized by paediatricians. Many infected infants presenting with milder symptoms are not identified and offered appropriate therapy and follow-up. In order to optimize outcomes for infants with cCMV, routine screening may need to be considered as a public health policy.

## Principal investigator

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## Acknowledgements

Results are dedicated in memoriam to Drs. Victor Marchessault and Susan King for their vision and support.

## Publications and presentations

Vaudry W, Lee BE, Rosychuk R, Pelletier L. Congenital cytomegalovirus infection in Canada: Cases reported by pediatricians to the Canadian Paediatric Surveillance Program. Canadian Paediatric Society Annual Conference, Victoria, BC, June 2008. (Oral presentation)



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

March 2005 to February 2008 – Final report

## Highlights

- The study confirmed 220 incident cases of head injury secondary to suspected child maltreatment.
- Of the confirmed cases, 140 had a diagnosis of suspected shaken baby syndrome, 75 had mild-to-severe neurological sequelae and 27 died as a result of injuries.
- The majority (75%) were under one year of age, with 58% under six months of age.
- Child welfare authorities had previously been involved in 31% of confirmed cases.

## Background

Despite the fact that the term “battered child syndrome” was first used in 1962, the study of child maltreatment is still in its infancy in Canada. 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 professionals identify children at risk and the process that is followed to protect those children.

Cases of inflicted head injury, although thankfully reasonably rare, are of great clinical importance, as a large proportion of them result in death or permanent neurological deficits.

Attempts have been made to quantify the issue in Canada; however, the information is limited. One effort was a retrospective study examining only shaken baby syndrome and the other was limited to cases where determination of physical harm was made by child welfare workers. The Canadian *Joint Statement on Shaken Baby Syndrome* (2001) recommended surveillance and collection of data on inflicted head injury.

## Objectives

- 1) Describe the incidence of head injury secondary to suspected child maltreatment (abuse or neglect) among Canadian children
- 2) Describe the incidence of head injury secondary to suspected child maltreatment in at-risk groups among the Canadian paediatric population
- 3) Identify the presentation, patterns and burden of head injury secondary to suspected child maltreatment

- 4) Inform strategies to improve protection of children and youth and provide an opportunity to educate health care professionals

## Case definition

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

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

- \* Neglect/failure to protect: the child has suffered harm or the child's safety or development has been endangered as a result of the caregiver(s)' failure to provide for or to protect the child. Please note that the term 'neglect' is not used in some provincial/territorial statutes, but interchangeable concepts include: failure to care and provide or supervise and protect; does not provide, refuses or is unavailable or unable to consent to treatment.
- a. Failure to supervise or protect leading to physical harm: the child suffered or is at substantial risk of suffering physical harm because of the caregiver's failure to supervise and protect the child adequately. Failure to protect includes situations in which a child is harmed or endangered as a result of a caregiver's actions (e.g. drunk driving with a child or engaging in dangerous criminal activities with a child).

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

## Results/discussion

TABLE 8

Head injury secondary to suspected child maltreatment cases from March 1, 2005 to February 28, 2008

Year	Reported	Duplicates	Excluded	Pending	Confirmed
2005*	111	30	13	5	63
2006	112	39	7	8	58
2007	149	19	24	14	92
2008†	22	4	7	4	7
<b>Total</b>	<b>394</b>	<b>92</b>	<b>51</b>	<b>31</b>	<b>220</b>

\* March 1 to December 31, 2005

† January 1 to February 28, 2008

### Demographic data

Of the 220 cases confirmed from 2005 to 2008, 33% were from the Western provinces (BC, AB, SK and MB), 60% were from Central Canada (ON and QC), 6% were from Eastern Canada (NS and NL) and 1% was from Northern Canada (NT). The median age at initial presentation was five months (n=194, range 1 week–10.5 years old). Of the confirmed cases, 75% (145/193) involved children under the age of one year and 58% (112/193) involved children less than six months of age. Boys represented 58% of the cases, girls 41% and the gender was not reported in 1%. Of those cases where the number of children in the household was reported (n=193), the median number of children was two (range 1–8 children).

### Management

Of the 220 confirmed cases, 76% initially presented to the emergency department, with the remainder presenting to a family physician or paediatrician. The initial presentation included decreased consciousness (36%), soft tissue injury (30%), seizure (29%), irritability (25%), vomiting (24%), lethargy (28%), apnea (15%) and respiratory difficulty (14%). Of the confirmed cases, 93% were hospitalized and 52% of these required care in the intensive care unit (ICU). Data on length of stay were available for 157 cases, with a median

length of stay of 10 days (range 1–392 days). Data on length of stay in the ICU were available for 61/115 cases admitted to the ICU with a median length of stay of three days (range 1–35 days). A hospital child protection team was involved in 94% of the cases and police were involved in 84% of the cases. Child welfare authorities had previously been involved in 31% of the confirmed cases.

### Injuries

Clinical findings were documented in all but one case and included:

- Subdural hematoma (71%)
- Seizures (32%)
- Retinal hemorrhage (51%)
- Skull fractures (37%)
- Bruising (39%)
- Cerebral edema (27%)
- Fractures of long bones or ribs (30%)
- Cerebral contusion (20%)
- Focal neurological findings (18%)
- Subarachnoid hematoma (17%)
- Abrasions (11%)
- Epidural hematoma (7%)
- Abdominal injuries (2%)

Previous medical history was reported for 82 of the cases. The most frequent issues were excessive crying (22%), prematurity (22%), developmental delay (16%), previous maltreatment (15%) and feeding difficulty (14%). Shaken baby syndrome was the suspected diagnosis in 64% of the cases, while “other physical abuse” accounted for 49% and neglect for 7%. Of note, multiple diagnoses were reported in some cases. Medical status at time of discharge was available for 193 cases: in 27 of these cases (14%) the injuries resulted in death, in 75 cases (39%) there were mild-to-severe neurological sequelae and in 91 cases (47%) the medical status at discharge was normal.

### Perpetrator

Perpetrator status was confirmed in 29/220 (13%) of cases, suspected in 95/220 (43%) and unknown in 96/220 (44%). The confirmed or suspected perpetrator was male in 66% of the cases. Moreover, in 71% of the cases the confirmed or suspected perpetrator lived with the child. The relationship of the confirmed or suspected perpetrator to the



child was available for 115 cases. In 70% of these cases the confirmed or suspected perpetrator was a parent and in 7% of cases it was a babysitter. Almost half (47%) of the confirmed or suspected perpetrators had a history of at least one risk factor, with the most common risk factors being domestic violence, few social supports, and drug and alcohol abuse.

## Conclusion

Results from this study show that, in children up to 14 years of age inclusively, there were 220 confirmed cases of head injury secondary to suspected child maltreatment (abuse or neglect) with over half presenting at less than six months of age and 75% of the cases at less than one year. Paediatricians suspected shaken baby syndrome in 64% of the confirmed cases. There was significant mortality and morbidity among confirmed cases. In the 193 cases where the outcome was known at the time of discharge, 27 (14%) died and 75 (39%) had mild-to-severe neurological sequelae. Most cases required intensive hospital resources indicating significant economic costs.

Infants, particularly those with excessive crying, prematurity, developmental delay or feeding difficulties appear to be particularly at risk. The fact that the child welfare authorities had previously been involved in 31% of these cases reinforces the importance of support for and close follow-up of at-risk families.

The increasing awareness of abusive head injury in infancy, its devastating consequences for children and their families, societal cost and its potential for prevention indicates the need for more effective prevention efforts within the first year of life.

## Principal investigator

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- Morag Mackay, MSc, BScN, European Child Safety Alliance
- Katherine Moreau, PhD(c), Children's Hospital of Eastern Ontario
- Amy Plint, MD, Children's Hospital of Eastern Ontario
- Michelle Ward, MD, Children's Hospital of Eastern Ontario

## Publications and presentations

Bennett S, Grenier D, Medaglia A. The Canadian Paediatric Surveillance Program: A framework for the timely data collection on head injury secondary to suspected child maltreatment. *Am J Prev Med* 2008;34(4S):S140–2

Shouldice M, Ward M. Recent headlines in the news: Controversies in inflicted head trauma. Canadian Paediatric Society Annual conference, Ottawa, ON, June 2009. (Oral presentation)

Bennett S, Fortin G, Ward M. The extent and nature of head injury secondary to child maltreatment in Canada: A 3-year surveillance study. Seventh North American Conference on Shaken Baby Syndrome/Abusive Head Trauma, Vancouver, BC, October 2008. (Oral presentation)

# Medium-chain acyl-coenzyme A dehydrogenase deficiency

September 2005 to August 2008 - Final report

## Highlights

- Three years of MCAD deficiency surveillance confirmed 46 incident cases.
- Newborn metabolic screening programs detected 74% of cases; all were asymptomatic.
- Two cases were diagnosed after death; none from provinces with newborn screening programs.

## Background

Medium-chain acyl-coenzyme A dehydrogenase (MCAD) deficiency is the most common autosomal recessive fatty acid oxidation disorder. The incidence is about one in 10,000–20,000. The commonest presentation is during infancy when a well child decompensates during an acute illness and develops hypoglycemia, vomiting and altered sensorium. Twenty-five percent (25%) of patients die at the time of the initial presentation. Some individuals with this disorder also remain asymptomatic, thus there is a great clinical phenotypic variability.

Treatment involves avoidance of fasting and ensuring adequate glucose intake during acute illnesses. Carnitine supplements have been used in MCAD deficiency patients; however, there is controversy about its prolonged use. At the start of the study, British Columbia, Saskatchewan, Nova Scotia, and Prince Edward Island were screening for this disorder. MCAD deficiency has an excellent prognosis when treated early and has genetic implications for future pregnancies and other family members.

## 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
- 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

TABLE 9

Medium-chain acyl-coenzyme A dehydrogenase deficiency cases from September 1, 2005 to August 31, 2008

Year	Reported	Duplicates	Excluded	Pending	Confirmed
2005*	3	0	1	0	2
2006	18	3	0	0	15
2007	30	11	3	2	14
2008†	20	1	2	2	15
<b>Total</b>	<b>71</b>	<b>15</b>	<b>6</b>	<b>4</b>	<b>46</b>

\* September 1 to December 31, 2005

† January 1 to August 31, 2008

## Discussion

The estimated incidence of MCAD deficiency is 14 cases per year in Canada. This appears to be lower than the initial estimate of 30 new cases per year. This could be due to under-reporting or lack of uniform newborn screening throughout Canada. To enhance case ascertainment, Canadian pathologists, particularly coroners and metabolic laboratory directors, participated in the study.

All cases detected on newborn metabolic screening, 34/46 (74%), were asymptomatic. Another 4/46 cases (9%) were identified through family screening after an index patient was diagnosed. Lastly, 8/46 cases (17%) presented with clinical symptoms. Of the 46 confirmed cases, 23 (50%) were homozygous for the 985 A>G mutation; however, not all centres have carried out the mutation analysis. The study confirmed two deaths, none from provinces where newborn metabolic screening was implemented. One of the two deceased patients was homozygous for the 985 A>G mutation.

## Conclusion

The study confirms the efficacy of newborn metabolic screening for detecting asymptomatic MCAD deficiency cases and for identifying other asymptomatic cases through family screening. Early diagnosis allows for implementing simple measures, such as preventing fasting and ensuring glucose intake during acute illnesses, to reduce the risk of severe illness and death.

The study reinforces the importance of ongoing education for paediatricians and health care providers, as MCAD deficiency has very variable clinical phenotypes.

At the launch of the study, only four provinces (BC, SK, NS, PE) had established systematic neonatal metabolic screening programs, and this has since grown to eight provinces (BC, AB, SK, ON, NB, NS, PE, NL) and one territory (YT).

The results of the study reinforce the importance of initiating newborn screening for MCAD deficiency

in the remaining Canadian provinces and territories, as MCAD deficiency has an excellent prognosis once the diagnosis is made.

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## Acknowledgements

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## Publications and presentations

Prasad C, Speechley KN, Dyack S, Rupa CA, Chakraborty P, Kronick JB. The expanding spectrum of medium chain acyl-coenzyme A dehydrogenase deficiency from trait to lethality: MCADD experience using the Canadian Paediatric Surveillance Program. Canadian Paediatric Society Annual Conference, Ottawa, ON, June 2009. (Poster presentation)

Prasad C, Speechley KN, Dyack S, Rupa CA, Chakraborty P, Kronick JB. Incidence of medium chain acyl-coenzyme A dehydrogenase deficiency in Canada using the Canadian Paediatric Surveillance Program (September 2005 to September 2008). Canadian College of Medical Geneticists Annual Scientific Meeting, St. John's, NL, September 2008. (Poster presentation)

# Non-type 1 diabetes mellitus

April 2006 to March 2008 – Final report

## Highlights

- Nearly 65% of all NT1DM cases are type 2 diabetes mellitus (T2DM).
- Obesity/overweight appears to be the single most important risk factor for T2DM.
- At diagnosis, nearly 40% of children with T2DM had at least one obesity-related co-morbid condition.
- Children developing medication-induced diabetes mellitus do not always have risk factors that are associated with type 2 diabetes.
- Study results identify the need for national randomized control trials of efficacy and safety of various treatment modalities for T2DM in the paediatric population.

## Background

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

Data on the incidence and prevalence of T2DM in Canadian children are limited. There is a global effort to conduct epidemiological studies to quantify the extent of the problem. Canadian-specific data are essential because of Canada's unique ethnic, cultural, geographic and behavioural characteristics. In addition to the participation of all paediatricians enrolled in the CPSP (n=2,560), this study included a sample of family physicians (n=98) and adult endocrinologists (n=48) in order to maximize case ascertainment.

## Objectives

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

## Case definition

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

Clinical features suggestive of NT1DM include:

- Obesity (body mass index > 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

**TABLE 10**

**Non-type 1 diabetes cases reported by paediatricians from April 1, 2006 to March 31, 2008**

Year	Reported	Duplicates	Excluded	Pending	Confirmed
2006*	167	11	17	22	117
2007	201	6	23	12	160
2008†	55	1	10	2	42
<b>Total</b>	<b>423</b>	<b>18</b>	<b>50</b>	<b>36</b>	<b>319</b>

\* April 1 to December 31, 2006

† January 1 to March 31, 2008

From April 1, 2006 to March 31, 2008, a total of 467 cases of NT1DM were reported, 423 cases by paediatricians (Table 10) and 44 by family physicians or adult endocrinologists. Of the confirmed cases, 266 (77%) were reported by paediatric endocrinologists, 53 (15%) by paediatricians, 22 (6%) by family physicians and 4 (1%) by adult endocrinologists. Table 11 provides the classification of all confirmed cases (n=345).

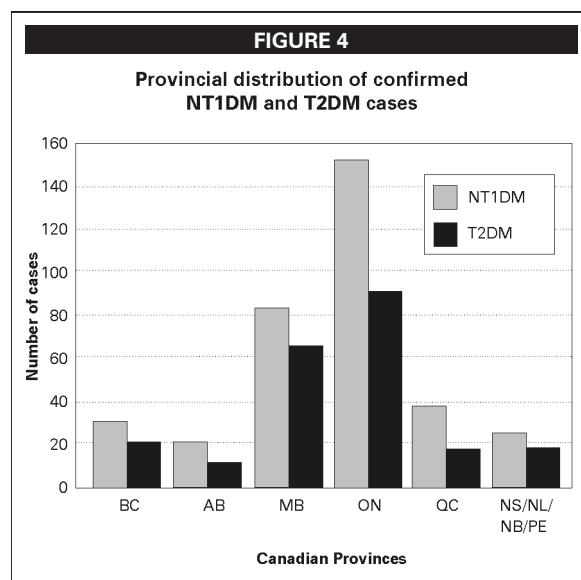
**TABLE 11**

**Classification of all confirmed cases of non-type 1 diabetes mellitus April 1, 2006 to March 31, 2008**

Confirmed	T2DM*	MID†	Monogenic DM	Indeterminate
345	227	56	31	31

\* Type 2 diabetes mellitus

† Medication-induced diabetes



Note: No confirmed cases from Saskatchewan and the territories.

Reporting of NT1DM varied across Canada. Figure 4 shows the provincial distribution of the confirmed cases of NT1DM and T2DM. Ontario and Manitoba had the highest rates of reporting.

### Clinical Features and Management of T2DM

Children with T2DM presented at a mean age of  $13.7 \pm 2.5$  years and 58% of cases were female. Ninety-five percent (95%) of children with clinically diagnosed T2DM were obese. At diagnosis, nearly 40% of children with T2DM had at least one obesity-related co-morbid condition with hypertension and dyslipidemia being the most common. Most children with T2DM had a positive family history of diabetes and many belonged to high-risk ethnic groups. The study found that roughly half of the children with T2DM were Aboriginal, but interestingly, other ethnic groups made up for the other half, with Caucasian representing 25% of this latter percentage. The treatment of T2DM varied considerably across the country. The most commonly used treatment modalities were: lifestyle counselling alone (33%), insulin therapy plus lifestyle counselling (28%) and a hypoglycaemic agent plus lifestyle counselling (21%).

Children developing medication-induced diabetes mellitus do not always have risk factors that are associated with type 2 diabetes. Lastly, the majority of children with monogenic diabetes are Caucasian and of normal weight. The specific NT1DM type could be identified in over 90% of confirmed cases.

## Discussion

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



These data underscore the critical need for primary prevention programs targeted towards childhood obesity, which are essential in the prevention of T2DM and other obesity related co-morbidities. As rates of childhood obesity and T2DM increase, MID may also occur more frequently, mediated directly or indirectly by increased body weight.

## Conclusion

This is the first study in Canada to measure and report the incidence of T2DM and other forms of NT1DM in children. Furthermore, this study demonstrates the feasibility of conducting national surveillance of a paediatric condition among a varied group of health professionals. This study is vital in providing epidemiological and demographic data on Canadian children affected with NT1DM and, specifically, obesity-related T2DM. This study shows that T2DM is a disease that does affect children and youth and appears to be increasing in frequency over time. Additionally, children and youth who develop MID do not always have risk factors that are known to occur in youth with T2DM. Lastly, the majority of children with monogenic diabetes are Caucasian and of normal weight.

These data will provide a foundation upon which specific paediatric health promotion and disease prevention programs can be established. For example, prevention strategies for T2DM in childhood should be targeted at all communities since almost 50% of children with clinically diagnosed T2DM are non-Aboriginal. These results also provide data 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. This study allows for future comparison of epidemiological data, recognition of national trends, and the assessment of the efficacy of health promotion and disease prevention programs. Lastly, the Canadian incidence rate of NT1DM, and specifically obesity-related T2DM, can be compared to other countries through collaboration with international surveillance units (e.g., the British Paediatric Surveillance Unit). Support from reporting physicians for the duration of this study is greatly appreciated by all investigators and collaborators.

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## Publications and presentations

Amed S, Dean HJ, Panagiotopoulos C, Sellers AC, Hadjiyannakis S, Laubscher TA, Dannenbaum D, Shah BR, Booth GL, Hamilton JK. National surveillance for non-type 1 diabetes mellitus in Canadian children: Type 2 diabetes, medication-induced diabetes, and monogenic diabetes. (Submitted for publication)

Hamilton J, Dean H, Amed S, Lambert-Lanning A, Laubscher T, Dannenbaum D. Sentinel network collaboration for pan-Canadian surveillance of NT1DM. Family Medicine Forum, Toronto, ON, November 2008. (Oral Presentation)

Amed S, Dean H, Hamilton J, NT1DM Study Team. National surveillance for non-type 1 diabetes (NT1DM) in Canadian children. CDA/CSEM Professional Conference and Annual Meetings, Montreal, QC, October 2008. (Oral Presentation)

Dean H. Type 2 diabetes in children and youth. Family Medicine Forum, Winnipeg, MB, November 2007. (Oral presentation)

Amed S, Dean H, Hamilton J and the Non-Type 1 DM Study Team. National surveillance for non-type 1 diabetes in Canadian children. Canadian Association for Health Services and Policy Research Annual Meeting, Toronto, ON, June 2007. (Oral presentation)

Amed S, Dean H. The changing landscape of diabetes in Canadian children. Canadian Paediatric Society Annual Conference, Montreal, QC, June 2007. (Oral presentation)

Amed S, Dean H, Hamilton J and the Non-Type 1 DM Study Team. National surveillance of non-

type 1 diabetes (NT1DM) in Canadian children. Canadian Paediatric Society Annual Conference, Montreal, QC, June 2007. (Poster presentation)

Amed S, Dean H, Hamilton J and the Non-Type 1 DM Study Team. Risk factors for type 2 diabetes in youth with medication induced diabetes. Canadian Paediatric Society Annual Conference, Montreal, QC, June 2007. (Poster presentation)

Amed S, Dean H, Hamilton J and the Non-Type 1 DM Study Team. Risk factors for type 2 diabetes in youth with medication induced diabetes. Pediatric Academic Society Scientific Meeting, Toronto, ON, May 2007. (Poster presentation)

# Transfusion-related acute lung injury

September 2005 to August 2008 – Final report

## Highlights

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

## Background

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

The incidence of TRALI in the paediatric population is unknown. Even though TRALI is becoming recognized more frequently in clinical practice and is receiving greater attention and description in the literature, it likely remains under-diagnosed and under-reported. This study is the first to assess the incidence, presentation and burden of TRALI in the paediatric population. Collecting national epidemiological data in the paediatric population helps 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 12

Transfusion-related acute lung injury cases  
from September 1, 2005 to August 31, 2008

Year	Reported	Duplicates	Excluded	Pending	Confirmed
2005*	0	0	0	0	0
2006	3	0	0	1	2
2007	1	0	0	0	1
2008†	1	0	0	0	1
<b>Total</b>	<b>5</b>	<b>0</b>	<b>0</b>	<b>1</b>	<b>4</b>

\* September 1 to December 31, 2005

† January 1 to August 31, 2008

## Discussion/conclusion

During the three years of surveillance, five cases were reported to the TRALI study and four cases were confirmed (Table 12).

The confirmed cases presented all the TRALI inclusion criteria: 1) occurrence within six hours of the transfusion; 2) ALI with acute hypoxemia, bilateral infiltrates on chest X-ray, without evidence of cardiac dysfunction; and 3) no pre-existing ALI. One case has to be considered as a possible TRALI since the patient underwent cardiopulmonary bypass in the six hours preceding the TRALI (alternative risk factor for ALI).

Although only four cases occurred and we cannot draw any statistical results from such few numbers, we can highlight certain facts:

- 1) Patients were mainly males (3/4) and less than one year old (3/4).
- 2) All patients had received multiple transfusions prior to the TRALI event.

3) All cases of TRALI were due to red blood cell transfusions.

4) Blood volume given varied between 6 and 15 cc/kg.

5) All TRALI events were reported to the blood banks.

6) Clinical symptoms present, besides dyspnea, were fever in two cases and tachycardia in one case; there was no hypotension.

It is important to specify that among the four patients, three were already in the paediatric intensive care unit when the TRALI occurred, which means that these patients could have been at higher risk for TRALI. More importantly, two patients were neonates with congenital cardiopathy who underwent cardiac surgery with cardiopulmonary bypass. The possibility that this population is at higher risk of TRALI should be addressed in future studies.

Another important point is the different degree of severity of TRALI. In two cases, TRALI was easily managed with oxygen and did not present further complications. In two other cases, TRALI was life-threatening and necessitated aggressive treatment with mechanical ventilation. In one of those cases, high frequency ventilation as well as nitric oxide was necessary and the TRALI was complicated with a pneumothorax. This demonstrates the wide range of severity that can be attributed to TRALI. Risk factors to explain the severity of TRALI could not be evaluated with this study. This should also be addressed in future studies.

Even though TRALI is becoming recognized more frequently and has received greater attention in the literature, very few cases of TRALI were reported during the study. Nevertheless, it was expected that more cases would have been reported. A compounding factor is that TRALI presents as a clinical syndrome without a pathognomonic confirmatory laboratory test; therefore, under-diagnosis and under-reporting are highly suspected, especially in children. Other possible reasons for the rarity of cases include the following:

- 1) The TRALI definition is not suitable in paediatrics, as it could be more difficult to evaluate ALI in small children.

- 2) The exclusion criteria discounting patients with previous ALI is restrictive and might exclude many neonates and paediatric intensive care unit patients that are more at risk.
- 3) The pathophysiology is different in children and their transfusion-related respiratory distress is mostly due to an etiology other than TRALI (i.e., cytokines).

Finally, TRALI is a very rare phenomenon and the incidence in the paediatric population remains unknown. This study constituted a useful tool to promote education and awareness among health care professionals of this uncommon transfusion reaction. Information on TRALI helps paediatricians to better recognize this serious life-threatening complication and to acknowledge the need to immediately alert the blood bank to prevent further distribution of the same donor blood to other patients, thereby avoiding further TRALI episodes.

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### **Publications and presentations**

Gauvin F, Hume H, Delage G, Robillard P, Fergusson D, Froese N, Lau W, Webert K, Whyte RK. Transfusion-related acute lung injury in the Canadian paediatric population. Canadian Paediatric Society Annual Conference, Ottawa, ON, June 2009. (Poster presentation)

# Acute flaccid paralysis

January 1996 to December 2010

## Highlights 2008

- A 2007 case of an imported vaccine-associated paralytic poliomyelitis case was reported in 2008.
- This serves as an important reminder that poliovirus infection has to be ruled out for each AFP case, ensuring that potential import or import-associated cases are rapidly detected and managed.
- Vigilant surveillance is essential as several countries have ongoing wild poliomyelitis outbreaks and many countries continue to use oral polio vaccine.
- Canada's AFP surveillance continues to work towards the WHO targets for AFP detection, stool specimen collection and follow-up for residual paralysis.

## Background

Elimination of indigenous wild poliovirus transmission was certified in Canada, and the rest of the American region, in September 1994. However, until global eradication of poliomyelitis is achieved, there remains an ongoing risk for importation of wild polioviruses. In 2008, endemic circulation of wild polio virus continued in four countries: Afghanistan, India, Nigeria and Pakistan. As of January 6, 2009 there were 1,618 cases of wild poliovirus reported from a total of 18 countries worldwide in 2008, compared with 1,317 during 2007. Consequently, active surveillance with appropriate follow-up investigation of acute flaccid paralysis (AFP) in children less than 15 years of age continues to be used to monitor for potential cases of paralytic poliomyelitis. This important activity is Canada's safeguard in maintaining vigilance for potential import or import-associated cases of paralytic poliomyelitis. As well, documentation of AFP monitoring and investigation activities is the means by which Canada is able to maintain its polio-free certification status.

## Objectives

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

- 1) Ability to detect at least one case of non-polio AFP (including Guillain-Barré syndrome

[GBS]) per year for every 100,000 children less than 15 years of age

- 2) Collection of adequate stool specimens for poliovirus examination from at least 80% of AFP cases within 14 days of the onset of paralysis
- 3) Completion of follow-up exams at least 60 days after paralysis onset to verify the presence of residual paralysis in at least 80% of AFP cases

## Case definition

Acute onset of focal weakness or paralysis characterized as flaccid (reduced tone) without other obvious cause (e.g., trauma) in children less than 15 years of age. Transient weakness (e.g., post-ictal weakness) does not meet the case definition.

## Results/discussion

As the study is ongoing, AFP delayed reports are received yearly and the figures are adjusted accordingly. Importantly, a 2007 case of an imported vaccine-associated paralytic poliomyelitis case secondary to an oral poliovirus immunization received outside Canada was reported in 2008. This serves as an important reminder that poliovirus infection has to be ruled out for each AFP case, ensuring that potential imported or vaccine-associated cases are rapidly detected and appropriately managed.

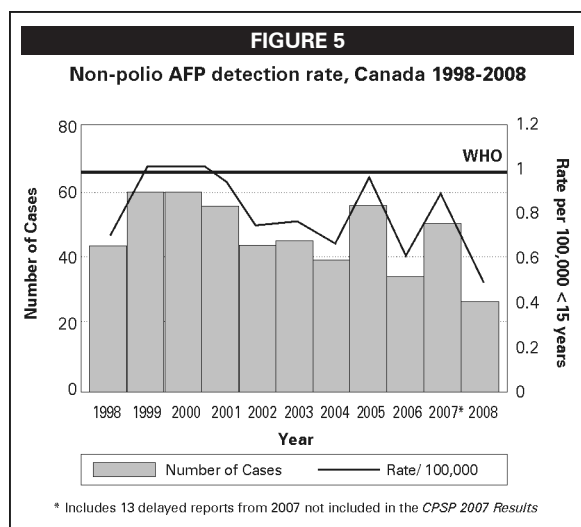
TABLE 13

Acute flaccid paralysis cases in 2008

Reported	Duplicates	Excluded	Pending	Confirmed
41	0	7	7	27

There were 41 reports of AFP with onset in 2008, including 27 confirmed cases (Table 13). The majority of confirmed cases (56%) were submitted from an IMPACT site, with the remainder originating from the CPSP. More than half of confirmed cases (63%) were reported from Ontario and Quebec.

Seven AFP reports were excluded: four based on age criteria and three did not meet the case definition. The 27 confirmed cases in 2008 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. The annual AFP incidence rate may be artificially low due to delays in receiving detailed questionnaires, seven of which were still pending (Figure 5).



#### Importance of stool investigation:

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

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

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

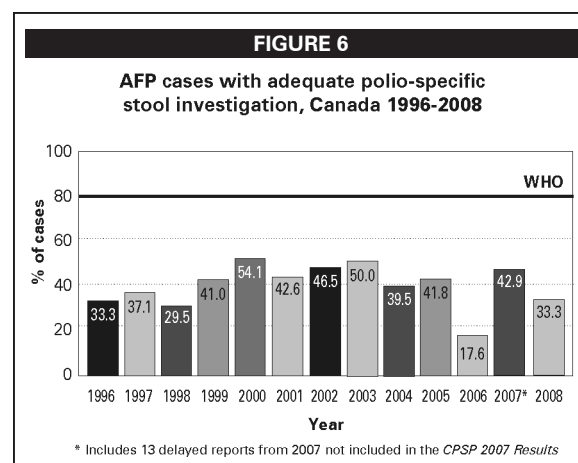
In 2008, AFP cases ranged in age from five months to 14 years (median seven years, mean 7.2 years),

and were fairly evenly distributed across the age groups. The male/female ratio was 2:1.

Only eight (30%) AFP cases had documented receipt of age-appropriate polio immunization with inactivated poliovirus vaccine. Four additional cases had polio vaccination information reported as “up-to-date” but with no accompanying details. The remainder of cases (15/27) were partially vaccinated or unvaccinated.

#### Investigation for polio virus, other enteroviruses or *Campylobacter*

Virological investigation included collection and testing of stool specimens for 13 cases (48%), cerebrospinal fluid (CSF) for 13 cases (48%), throat swabs for 14 cases (52%) and polio-specific serology for one case (4%). Where stool was collected, 9/13 cases (69%) had adequate investigation for isolation of poliovirus within two weeks of the onset of paralysis. In the remaining four cases, stool collection was later, when the sensitivity of virus isolation is decreased. Rates of adequate stool investigation have been consistently below the WHO surveillance target of 80% (Figure 6). While there was no positive identification of polioviruses from any of the virological investigations, one case had rotavirus isolated as a possible cause of AFP. Testing for *Campylobacter* was done in seven (26%) cases, and was not isolated in any of the samples.



#### Neurological investigations

In 2008, approximately 89% of cases underwent at least one type of neurological investigation

(CSF examination, nerve conduction studies/electromyography, MRI/CT scan) with all three types conducted equally often. In the remaining 11% of cases, investigations were not reported. CSF chemistry showed abnormalities in 13/17 cases (77%). Electromyography and/or nerve conduction studies showed abnormalities in 7/12 cases (58%). MRI or CT scans showed abnormalities in 13/20 cases (65%).

As observed in previous years, the majority of AFP cases (n=16, 59%) were diagnosed as GBS, one of which was Miller-Fisher variant. In 2008, the 11 “other” diagnoses, included transverse myelitis (n=7), viral encephalopathy (n=2), infantile botulism (n=1) and juvenile idiopathic arthritis (n=1).

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

All AFP cases reported in 2008 required hospitalization, with lengths of stay ranging from one to 60 days (average 13 days). For three cases, the lengths of stay were unknown. Outcome at the time of the initial report was documented in 26 cases: three (12%) fully recovered, 19 (73%) partially recovered with residual weakness or paralysis and four (15%) did not recover but reported as improving. Only twelve cases (44%) had status at 60 days reported, including five cases who had fully recovered, four with partial recovery/some residual weakness or paralysis and three with outcomes pending. This is below the 80% WHO recommended target for high quality AFP surveillance and may be impacted by the timing of report completion/submission.

### **Conclusion**

A total of 27 AFP cases were confirmed, giving a national non-polio AFP detection rate of 0.48/100,000, below the WHO target which has been met only twice (in 1999 and 2000) since AFP surveillance began in 1996. This is despite seemingly sensitive surveillance through the CPSP and IMPACT networks. Canada’s lower than expected AFP rates may be a result of under-detection of cases in combination with delayed reporting or it may be a true reflection of lower baseline levels for non-polio AFP in Canada and other developed countries.

The vast majority of reported AFP cases continue to undergo one or more neurological investigations. Given that most AFP cases are diagnosed as either GBS or transverse myelitis, clinical signs and symptoms consistent with these conditions may favour neurological investigations. However, polio-specific laboratory investigations remain vital for WHO recommended evaluation and documentation of all cases, including those in which poliomyelitis is considered a very low possibility.

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

### ***Global polio eradication initiative***

Despite some continuing challenges, global polio eradication was reaffirmed by the Advisory Committee on Polio Eradication (Geneva, 2005) and at the World Health Assembly (Geneva, 2006). While just over 1,618 cases of poliomyelitis were reported globally in 2008, 92.5% of these occurred in four countries where indigenous polio transmission is still occurring: Nigeria, India, Pakistan and Afghanistan. For polio-free countries (such as Canada), the 2007 case of an imported vaccine-associated paralytic poliomyelitis reported in 2008 and Australia’s July 2007 detection of a case of wild type poliomyelitis in a 22-year-old student returning from a visit to Pakistan, serve as reminders of the possibility of importation. This is particularly important for industrialized nations where indigenous poliovirus circulation has long since been eradicated. The risk of disease importation is real and all countries must remain vigilant to rapidly detect and respond to possible imported cases. The Pan American Health Organization cautions that countries in the Americas may not be prepared to adequately

respond to a poliovirus importation if they are not conducting adequate and timely stool investigation to definitively rule out poliovirus infection in **all** AFP cases less than 15 years of age (and AFP *in any age* that could be due to poliovirus infection). All countries, including Canada, must maintain high quality AFP surveillance and high vaccine coverage.

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### Acknowledgements

The contribution of Jeannette Macey and Kelly Mansfield is greatly appreciated.

### Publications and presentations

Garner MJ, Macey JF, Desai S, Grenier D.

Ensuring our polio-free status: active acute flaccid paralysis surveillance (AFP) in Canada. Canadian Immunization Conference, Toronto, ON, December 2008. (Poster presentation)





# Adverse drug reactions – serious and life-threatening

January 2004 to December 2009

## Highlights 2008

- In 2008, the study confirmed 35 cases of suspected serious paediatric adverse reactions.
- Product groups most commonly associated with suspected adverse reactions were anti-infective agents, anticonvulsants and immunosuppressants.

## Background

Adverse drug reactions (ADRs) rank as one of the top 10 leading causes of death and illness in the developed world. Of particular concern is the alarming lack of understanding of ADRs in children. While children are known to be at greater risk than adults, there is a remarkable lack of understanding of causation and therefore a limited ability to avoid or prevent these occurrences. Health-related accreditation bodies estimate that 95% of all ADRs are not reported.

More than 75% of prescribed pharmaceuticals on the market in North America have never been tested in paediatric populations and are used without the benefit of adequate guidelines for safety or efficacy. Clinical practice has focused on adjusting dosage to account for smaller body mass, with the assumption that clinical effects would be equivalent to those observed in adults. It is now understood that a host of biological, developmental and behavioural factors affect the safety and effectiveness of pharmaceuticals when used in paediatric patients.

The CPSP ADR reports are submitted to the Canada Vigilance Program of the Marketed Health Products Directorate of Health Canada.

## Objectives

- 1) Determine the feasibility of an active surveillance system (CPSP) to identify serious and life-threatening paediatric ADRs not currently captured by existing spontaneous reporting systems
- 2) Identify the products most frequently causing ADRs in children, the type of reactions encountered and the characteristics of those affected

- 3) Determine the usefulness of the data collected for meaningful analysis and interpretation
- 4) Continue the reporting and monitoring of serious and life threatening adverse reactions collected through the CPSP

## Case definition

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

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

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

## Exclusions

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

## Results/discussion

TABLE 14

Adverse drug reaction- serious and life-threatening cases in 2008

Reported	Duplicates	Excluded	Pending	Confirmed
68	0	7	26	35

In 2008, 68 cases of suspected serious ADRs were reported and 35 were confirmed (Table 14), compared to 45 confirmed cases last year. The confirmed suspected serious ADR cases included 14 females, 20 males and in one case the sex of the

patient was not provided. The ages of the cases ranged from neonate (less than one month old) to 17 years. Patient age could not be determined in two reports. The majority of cases involved children five years and younger (n=15), followed by adolescents (n=11) and children six to 12 years (n=9). In comparison to 2007, the age distribution was n=9, n=18 and n=16 cases respectively.

Thirty-five reports were classified as serious by meeting the following criteria (more than one reason for seriousness was reported in nine reports): fatal outcome (n=3); life threatening (n=12); resulted in hospitalization or prolongation of hospitalization (n=21); or were considered medically important (n=12). A medically important reaction is defined as one that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the patient or may require intervention to prevent one of these other outcomes from occurring. In 2007, the distribution of the 45 ADR cases was very similar.

Information regarding patient outcome was provided for 31 of the 35 cases as follows: recovered (n=22); not yet recovered (n=5); recovered with sequelae (n=1); fatal outcome (n=3). The first fatal report involved an adolescent with Crohn's disease who developed a malignant hepatic tumor after several years of treatment with infliximab and azathioprine. The patient died of complications of carcinoma approximately one year after diagnosis. The second case involved a neonate who received fentanyl for analgesia pre-intubation. The infant experienced thoracic rigidity that led to desaturation and bradycardia and could not be resuscitated. In the third case, a pre-adolescent with autism and Tourette's syndrome died suddenly three days after abrupt discontinuation of olanzapine and sertraline.

The majority of cases had described dermatological reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis. All cases described reactions that were documented in standard drug reference sources for the health product except for three: unexplained death following discontinuation of olanzapine and sertraline; haemoglobin and red blood cell count increase suspected with the use of isotretinoin; and anaphylactic reaction

following a single intravenous bolus of phenytoin. The information source used for this determination was the Canadian approved product monograph. When an approved product monograph was not available, the source used was the Compendium of Pharmaceuticals and Specialties (CPS), electronic version, or the Micromedex™ Drug Information System.

### Suspected health products

Table 15 lists all health products suspected of causing ADRs in the 35 confirmed cases, sorted by the number of reports received for each individual product. In 29 cases, a single product was suspected of causing the reaction(s). Two suspect products were reported in five cases and one case listed three suspect products, two of which were intravenous solutions. The class of health products most frequently suspected was anti-infective agents (n=10), followed by anticonvulsants (n=9) and drugs classified as immunosuppressants or disease modifying antirheumatic drugs (n=4). These findings are similar to those seen in 2007, except that the third most frequently involved class of products was anti-neoplastic agents.

As in previous years, collaboration with Health Canada continues and completed ADR reports have been processed by the CPSP principal investigator and the Canada Vigilance Program of the Marketed Health Products Directorate of Health Canada, for detecting potential product-related safety issues and contributing to benefit-risk assessments of these products.

**TABLE 15**  
**Suspected or interacting health products**  
**in confirmed ADR cases in 2008**

Suspected health product	# Reports
Phenytoin	5
Carbamazepine, ceftriaxone, ibuprofen, ketotifen, minocycline	2 each
Acetazolamide, aminophylline, amoxicillin, atomoxetine, azathioprine, azithromycin, botulinum toxin A, cefazolin, cefprozil, clarithromycin, dextrose 5% injection, etoposide, fentanyl, fluticasone/salmeterol*, infliximab, isotretinoin, lamotrigine, leflunomide, lidocaine/prilocaine*, mercaptopurine, nitrofurantoin, normal saline injection, olanzapine, prednisone, propofol, sertraline, valproic acid	1 each

\* Combination products containing two active ingredients



## Conclusion

The class of health products most frequently suspected of causing the adverse reaction(s) was anti-infective agents, followed by anticonvulsants and immunosuppressants. All three classes of health products are frequently used in paediatric care. The majority of the ADR cases described dermatological reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis.

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

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

## Principal investigator

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## Acknowledgements

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## Publications and presentations

Zimmerman M, Rieder M. The power of adverse drug reaction reporting. Canadian Paediatric Society Annual Conference, Victoria, BC, June 2008. (Oral presentation)

# Bulimic eating disorders

March 2008 to February 2010

## Highlights 2008

- In the first 10 months of surveillance, 77 new cases of bulimic eating disorders were confirmed in children aged five to 18 years.
- At least one physical symptom of bulimia was found in 82% of confirmed cases.
- Of the confirmed cases, 88% were receiving regular medical monitoring.
- The most common (66%) mental health intervention was individual therapy.

## Background

Little is known about bingeing and purging disorders in young people. Bulimia nervosa (BN) occurs in 1% of the adolescent population with partial symptoms occurring in 3–6%. Mortality rates range from 0–6%. Alarming, only 4% of adolescent girls with bingeing and 6% of girls with purging reported being assessed or treated.

Few studies focus on the medical complications of BN in children and adolescents. There are many consequences of bulimia, including hypokalemia associated with cardiac arrhythmias, muscle weakness, gastrointestinal difficulties and dehydration.

Currently the diagnostic criteria for children are identical to those for adults, although there is evidence that children may differ significantly in their presentation.

There is little Canadian data on the incidence, presentation and medical complications of bulimia in children and adolescents. Collecting data through the CPSP is an efficient way to advance knowledge on the presentation, diagnosis and medical complications of this serious disorder.

## Objectives

- 1) Determine a conservative incidence rate of children and young adolescents presenting to paediatricians with bulimic eating symptoms and behaviours
- 2) Describe the bulimic behaviours and the associated physical symptoms in children and adolescents on presentation to a paediatrician
- 3) Identify psychiatric co-morbid disorders that accompany bulimic eating disorders

- 4) Describe the current treatment planned and/or offered to these children

## Case definition

Report any new patient presenting between the ages of five and 18 years (up to the 18<sup>th</sup> birthday) with bingeing and/or purging behaviour:

- Bingeing is characterized by eating, in a two-hour period or less, an amount larger than what most people would eat under similar circumstances and a sense of loss of control over eating during the episode.
- Purging can include: self-induced vomiting; misuse of laxatives, diuretics and other medications; and/or other inappropriate compensatory behaviours, such as fasting or excessive exercising.

## Exclusion criteria

Children who have biological causes for either bingeing or purging or who suffer from a psychotic disorder, or significant developmental delay

## Results

TABLE 16

Bulimic eating disorders cases  
from March 1 to December 31, 2008

Reported	Duplicates	Excluded	Pending	Confirmed
116	3	4	32	77

In the first 10 months of surveillance, 77 new cases of bulimic eating disorders were confirmed in children aged five to 18 years. The mean age of children presenting with bulimic eating disorder symptoms is 16 years (range 12–19). Twenty subjects were between the ages of 12 to 15 years

and 57 were between 16 to 19 years. Only one boy (1%) has been identified to date. The estimated incidence rate of children and young adolescents, aged five to 18 years, presenting with bulimic eating symptoms and behaviours was 1.4 per 100,000 (95% CI: 1.1–1.7/100,000).

Both bingeing and vomiting were found in 52 (68%) children. The breakdown of symptoms can be found in Table 17.

**TABLE 17**

**Eating disorder symptoms**

Symptom	Frequency (n=77) (Percentage)
Bingeing	58 (75%)
Vomiting	71 (92%)
Laxative abuse	15 (19%)
Diuretic abuse	3 (4%)
Other weight loss medication	15 (19%)
Exercise	52 (68%)
Food avoidance	67 (87%)
Fear of weight gain	71 (92%)
Preoccupation with food	69 (90%)
Preoccupation with body weight	70 (91%)
Perception that body is larger than it is	51 (66%)
Denial of severity of symptoms	31 (40%)
Somatic complaints	32 (42%)

Of the confirmed cases, 63 (82%) children presented with at least one physical symptom. A breakdown of the physical symptoms can be found in Table 18.

**TABLE 18**

**Other physical symptoms**

Symptom	Frequency (n=77) (Percentage)
Bradycardia	8 (10%)
Tachycardia	5 (6%)
Hypokalemia	6 (8%)
Dehydration	9 (12%)
Dizziness	39 (51%)
Syncope	11 (14%)
Decreased gastric motility	17 (22%)
Gastro-oesophageal reflux	7 (9%)
Blood in vomit	11 (14%)

Less than half of the children did not have a co-morbid mental health diagnosis, while 36% had one co-morbid diagnosis and 23% had two or more diagnoses. Thirty-six (47%) cases had a past history of a mental health disorder other than bulimia or binge eating and 52 (68%) had at least one family member with a history of a mental health disorder.

Management included regular medical monitoring for the majority of children (88%). However, five (6%) cases had no follow-up and two (3%) had medical or nutritional follow-up. Hospitalization occurred in 17 (22%) children. The most common mental health intervention was individual therapy (66%) followed by psycho-education (55%) and family therapy (49%). Only 25 (32%) subjects received a psychotropic medication.

Bingeing may be associated with sexual activity ( $p=0.059$ ) and multiple sex partners ( $p=0.052$ ). Vomiting may be associated with self-harm ( $p=0.61$ ) and impulsive behaviour ( $p=0.72$ ).

## Discussion/conclusion

The extremely low incidence rate (as compared to school-based surveys) suggests the possibility that very few children with bingeing and/or purging reach medical attention. Boys and younger children are apparently, extremely rare in this population. Important information and early patterns with differing associations for bingeing and purging are beginning to emerge, with some approaching statistical significance. These early results confirm the importance of collecting national epidemiological data over several years to ensure that an adequate sample size is obtained, allowing for meaningful interpretations of patterns of presentation and treatment.

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# Congenital myotonic dystrophy

March 2005 to February 2010

## Highlights 2008

- Three cases of CMD were confirmed in 2008, less than previous years and less than anticipated.
- None of the cases needed prolonged ventilation.
- No deaths were reported.

## Background

Myotonic dystrophy is an autosomal dominant multi-system disorder characterized by muscle weakness and myotonia commonly beginning in adulthood. There are two genetic loci for the disease but only one, DM1, is associated with congenital myotonic dystrophy (CMD). The DM1 mutation is a CTG trinucleotide repeat in the DMPK gene on chromosome 19. Myotonic dystrophy demonstrates genetic anticipation; a more severe phenotype is evident at an earlier age in successive generations. CMD manifests with hypotonia in the newborn associated with mechanical respiratory compromise and feeding dysfunction.

The current surveillance study is gathering information about the incidence of CMD and the number of children that are index cases for their families. Data are being collected for each individual case including clinical information and outcome, providing rates of mortality and morbidity. The study results will help health care providers and families obtain quality information on which to base care management decisions that arise in newborns with CMD, as well as raise awareness about CMD among Canadian paediatricians.

## Objectives

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

## Case definition

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

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

## Results/discussion

TABLE 19

Congenital myotonic dystrophy cases in 2008

Year	Reported	Duplicates	Excluded	Pending	Confirmed
2008	8	3	2	0	3

There were eight cases reported in 2008. Of these, three cases met the inclusion criteria and were confirmed as incident cases. The cases were reported from three different provinces and territories. Of the three confirmed cases, two were male and one was female. The children were all diagnosed before they reached one year of age. Table 19 demonstrates the number of duplicate and excluded cases. One reported case of CMD, which did not meet the inclusion criteria of requiring hospitalization for more than 72 hours, had only mild hypotonia with no respiratory or feeding difficulties and a CTG repeat length of 800.

All infants were born at term and, despite poor Apgar scores, cord gases were normal. No deaths occurred in 2008. None of the cases needed prolonged ventilation. All three children had hypotonia or feeding difficulties that led to prolonged hospitalization, ranging from nine to 71 days. Two of the three cases had respiratory difficulty but required oxygen for less than two days. All had feeding difficulties and required naso-gastric feeding therapy with a duration of two to 71 days. The children had CTG repeats of 900, 1,000 and 1,200. Other complications included vesicoureteral reflux, apneic spells, plagiocephaly, undescended testes and club foot.

Two children were the index cases for their families. In one case, the mother was aware of her CMD diagnosis and declined prenatal counselling or testing. In two cases, the mother and child had the same number of CTG repeats demonstrating the variability in the onset and severity of symptoms at the same CTG repeat level.

In addition to this surveillance study, an ongoing parallel natural cohort study is available to subjects.

## Conclusion

For the 2008 study period, the reported children had a relatively mild range of phenotypes, with feeding difficulties being the main cause of prolonged admission to hospital in the newborn period. Prolonged ventilation remains rare. The

CMD surveillance has confirmed 26 cases since beginning in 2005, which represents fewer cases than the expected 10–12 per year. Ongoing surveillance of CMD is important, as the impact of this disease is systemic, chronic, and often associated with significant morbidity and mortality in the newborn period.

## Principal investigator

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## Publications and presentations

Ho A, Campbell C. Medical morbidity and mortality in a population-based sample of congenital myotonic dystrophy. Muscle Study Group Meeting, Buffalo, NY, September 2008. (Poster presentation)

# Juvenile idiopathic arthritis

October 2007 to September 2009

## Highlights 2008

- In 2008, 354 cases of newly diagnosed JIA were confirmed.
- The most common JIA subtype is oligoarthritis.
- Children with JIA often have a delay in receiving a diagnosis.
- Children with First Nations ethnicity are over-represented amongst children with JIA.

## Background

Chronic arthritis in childhood, called juvenile idiopathic arthritis (JIA), is a rare chronic condition of children and adolescents. Although rarely fatal, the condition is long-term and associated with serious physical disability, pain, loss of independence, restrictions in daily activities and social participation, and unemployment as young adults.

Accurate data on the scope of chronic arthritis in children in Canada are scarce. This information is crucial to examining the gaps in health service provision. A limited number of epidemiologic studies have tried to measure the scope of JIA in Canada. Annual incidence rates have been reported between 5.3 and 10 per 100,000, with higher prevalence estimates of 32–52 per 100,000 calculated. These estimates were obtained from paediatric rheumatology specialty centres. Thus, although disease incidence is perceived as relatively low in Canada, there is the possibility of significant underestimation of the number of cases.

Measuring the scope and magnitude of JIA in Canada will support the development of health resources that can lead to improved quality of life for these children.

## Objectives

- 1) Ascertain the incidence of JIA in Canada
- 2) Determine feasibility and usefulness of an active surveillance system of JIA
- 3) Describe the demographics, including regional and ethnic variations of chronic childhood arthritis in Canada
- 4) Describe the clinical features of chronic childhood arthritis in Canada at presentation

- 5) Describe initial management strategies for chronic childhood arthritis in Canada, including treatment choices and referral strategies
- 6) Generate awareness of this rare disease among paediatric health care professionals

## Case definition

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

- Arthritis: persistent inflammation in one or more joints defined as:
  - ▶ Swelling or effusion, or
  - ▶ Presence of two or more of the following signs:
    - Limitation of range of motion
    - Tenderness on motion
    - Pain on motion
- Duration of disease:  $\geq 6$  weeks

## Exclusion criteria

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

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

## Results

TABLE 20

Juvenile idiopathic arthritis cases in 2008

Reported	Duplicates	Excluded	Pending	Confirmed
364	8	1	1	354

## Demographic and epidemiologic data

There were 354 confirmed cases of newly diagnosed JIA in 2008. The majority of cases were reported from Ontario (25%), followed by British Columbia



(19%), Alberta (16%), Quebec (15%), Nova Scotia/Prince Edward Island/Newfoundland/Labrador (14%), Manitoba (8%) and Saskatchewan (3%). No cases were reported from paediatricians in the territories; however, of the patients reported by paediatric rheumatology centres, three children were residents of the Northwest Territories or the Yukon. Prior to diagnosis, 20% of children were seen in an emergency room; 31% by a family doctor. Many children had consulted multiple health care providers prior to receiving a definite diagnosis of JIA. The median time from symptom onset to diagnosis was 4.3 months, with a range of 0–76 months.

Of the 354 confirmed cases, ethnicity data was available for 172 patients (49%). The majority of these patients (77%) were Caucasian. Other ethnicities included First Nations (7%) and Asian (7%). In 10% of cases, the ethnicity was marked as unknown. Where gender was identified, 59% of cases were girls and 35% were boys.

#### ***Clinical features at presentation***

Nearly 100% of patients were found to have joint pain, swelling or morning stiffness at diagnosis. The median number of affected joints at diagnosis was six (range 0–41). The most commonly affected joints were the knees, followed by the ankles and wrists.

#### ***JIA subtypes reported***

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

For the 211 patients with complete data, a subtype was assigned in 188 (89%) cases (Table 21). Of the 23 patients for whom a subtype was not assigned, 21 of these were reported by general paediatricians, and two by paediatric rheumatologists. The most common JIA subtype was oligoarthritis. Polyarthritis RF negative was the second most common subtype, followed closely by enthesitis-related arthritis. Although relatively rare,

a significant number of children with polyarthritis RF positive and systemic arthritis were reported.

**TABLE 21**

**Number of cases (n=188) and percentages of JIA subtypes**

JIA subtype	Number of cases (%)
Oligoarthritis	72 (34)
Enthesitis-related	38 (18)
Polyarthritis RF–	41 (19)
Psoriatic	7 (3)
Polyarthritis RF+	12 (6)
Systemic	8 (4)
Unclassified	10 (5)

## **Discussion/conclusion**

In 2008, 354 newly diagnosed cases of JIA were confirmed, with the majority of patients from paediatric rheumatology subspecialty centres. All provinces were represented, with a distribution relatively consistent with child population. Study data continue to show an over-representation of children from First Nations, consistent with similar reports of high incidence of arthritis in their adult counterparts.

Many children were seen by multiple health care providers prior to their final diagnosis of JIA, suggesting potential delays in diagnosis. In addition, the median time from symptom onset to diagnosis was four months; however, the range was broad. This demonstrates that many children with JIA in Canada have a long delay prior to receiving their diagnosis and beginning treatment.

To date, the clinical presentations of the patients in this study are consistent with previously published studies, showing joint pain, swelling and stiffness as being the most frequent manifestations. The most common JIA subtype is oligoarthritis. Enthesitis-related arthritis, a JIA subtype infrequently reported in epidemiologic studies, was documented in 18% of patients, making it relatively common. Systemic arthritis is a rare subtype of JIA, with few cases seen over the one-year period.

These data demonstrate that JIA is seen across Canada, but that cases are rarely reported from the northern regions. Children of First Nations heritage are at increased risk of JIA. This study is able to show trends of delay in diagnosis for children with JIA, delaying the early onset of treatment which

is known to be important for good long-term outcomes. The distribution of subtypes of JIA shows that enthesitis-related arthritis is an important subtype that requires intensive research.

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### Publications and presentations

Tucker LB, Dancey P, Oen K, Huber A, Lagacé C, Espinosa V, Canadian Alliance for Pediatric Rheumatology Investigators (CAPRI). Canadian national surveillance for juvenile idiopathic arthritis. *Arthritis Rheum* 2008; 58(suppl 9): Abstract 1228. Annual Scientific Meeting of the American College of Rheumatology, San Francisco, CA, October 2008. (Oral presentation)

# Kernicterus

January 2007 to December 2009

## Highlights 2008

- Kernicterus (chronic bilirubin encephalopathy) continues to occur in Canada.
- ABO incompatibility, G6PD deficiency and sepsis are the most common causes of acute bilirubin encephalopathy leading to kernicterus.
- The diagnosis of kernicterus in infants less than one year of age is based on clinical course, results of the auditory brain stem responses and MRI findings.

## Background

Hyperbilirubinemia remains the most common cause of neonatal hospital readmissions in Canada with the risk of acute bilirubin encephalopathy and kernicterus. Clinical features of chronic bilirubin encephalopathy include athetoid cerebral palsy, dystonia, hearing loss, dental dysplasia, oculomotor impairments and intellectual delays. On MRI, children with kernicterus can show increased signal intensity in the basal ganglia and the subthalamic nuclei.

Historically, kernicterus resulted from hemolysis and hyperbilirubinemia secondary to Rh isoimmunization and ABO incompatibility. Between the 1950s and 1980s, several developments resulted in a marked reduction of kernicterus, such as exchange transfusions, RhoGAM, testing of antibody titres during pregnancy, cord blood testing for blood group, antiglobulin antibodies (Coombs' testing) in neonates and phototherapy.

A recent Canadian surveillance study on severe hyperbilirubinemia demonstrated that ABO incompatibility followed by G6PD deficiency were the most common causes and that almost three-quarters of newborns were readmitted to hospital. With early detection of severe neonatal hyperbilirubinemia, both acute bilirubin encephalopathy and kernicterus could be prevented.

## Objectives

- 1) Establish the incidence of kernicterus and/or chronic bilirubin encephalopathy in Canada
- 2) Identify epidemiological and medical risk factors, possibly useful in preventing this disease, whether it is through selective screening of newborns for serum bilirubin, G6PD and Coombs' testing, or measuring serum bilirubin in all newborns prior to discharge from hospital

## Case definition

Report any child up to six years of age with:

- History of significant neonatal hyperbilirubinemia (peak bilirubin  $>425\mu\text{mol/L}$  or exchange transfusion) and
- Two or more of the following symptoms:
  - a) Extrapyramidal disorders (e.g., dystonia, athetosis)
  - b) Other movement disorder (spasticity or hypotonia)
  - c) Gaze abnormalities
  - d) Sensorineural hearing loss
  - e) Intellectual deficits
  - f) Enamel dysplasia of the deciduous teeth

OR

- Abnormal MRI with bilateral lesions of basal ganglia/midbrain (globus pallidus + subthalamic nucleus) with a history of neonatal hyperbilirubinemia

## Exclusion criteria

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

## Results/discussion

TABLE 22

Kernicterus cases in 2008

Reported	Duplicates	Excluded	Pending	Confirmed
11	2	0	7	2

In 2008, the study confirmed two cases of infants with kernicterus (chronic bilirubin encephalopathy). Seven cases from 2008 are still pending, awaiting the detailed questionnaires (Table 22). In two years of surveillance, the study has confirmed 14 cases. Interestingly, in all but one case, the diagnosis was established very young; less than one year of age. The range of peak bilirubin was 418–795  $\mu\text{mol/L}$  (mean 559  $\mu\text{mol/L}$ ). The etiologies included ABO incompatibility ( $n=3$ ), G6PD deficiency ( $n=2$ ), sepsis ( $n=2$ ), other antibodies ( $n=1$ ), Rh isoimmunization ( $n=1$ ), with pending G6PD results ( $n=1$ ). In four cases, the etiology was not available. Of the 14 confirmed cases, 12 (86%) had abnormal neurological findings. Hearing assessments were carried out by auditory brain stem testing ( $n=12$ ) (abnormal in 10 and normal in two). Confirmatory MRI scans of the brain were performed in 11 cases and all were abnormal.

Using this very conservative estimate of 14 new cases of kernicterus over a two-year period (assuming a birth rate of 300,000/year), the estimated incidence of kernicterus would be 1:43,000 births.

So far, study data have permitted the determination of the study objectives: specifically, the incidence estimate of kernicterus and the identification of the etiology in the majority of cases. The incidence estimate is very conservative given that reporting is voluntary and the establishment of kernicterus as a diagnosis is often difficult and may be delayed, both leading to under-reporting.

The most common etiologies for kernicterus were ABO incompatibility, G6PD deficiency and sepsis. This is in keeping with the previous CPSP surveillance study on severe neonatal hyperbilirubinemia in Canada. Information regarding the infant's blood group, Coomb's test and G6PD status is unknown at the time when most newborns are discharged home. Therefore, infants at risk of developing severe hyperbilirubinemia and subsequently kernicterus would not be identified in advance. This highlights the importance of careful monitoring for hyperbilirubinemia in newborns at the time

of discharge and in follow-up, as expressed in the updated Canadian Paediatric Society statement entitled, *Guidelines for detection, management and prevention of hyperbilirubinemia in term and late preterm newborn infants (35 or more weeks' gestation)*, published in June 2007.

The intent of the new guidelines is to identify at-risk newborns, to provide close supervision and early treatment, with the hope of reducing complications of hyperbilirubinemia. If the guidelines are effective then kernicterus should be prevented. Continued surveillance is needed to document the impact of the CPS clinical guidelines on the management of neonatal hyperbilirubinemia.

## Conclusion

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

Given that there have been changes to the CPS guidelines on the management of neonatal hyperbilirubinemia, continued surveillance is necessary to assess their effectiveness and whether additional strategies are needed to prevent kernicterus.

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## **Publications and presentations**

Sgro M, Campbell D, Shah V. The incidence of kernicterus in Canada 2007–2009. Canadian Paediatric Society Annual Conference, Victoria, BC, June 2008. (Oral presentation)

Sgro M, Campbell D, Barozzino T, Fallah S, Shah V. Severe neonatal hyperbilirubinemia and neurological findings in Canada. Canadian Paediatric Society Annual Conference, Victoria, BC, June 2008. (Oral presentation)

Sgro M, Campbell D, Shah V. The incidence of kernicterus in Canada 2007–2009. Pediatric

Academic Societies Annual Meeting, Honolulu, Hawaii, May 2008. (Poster presentation)

Sgro M, Campbell D, Barozzino T, Fallah S, Shah V. Severe neonatal hyperbilirubinemia and neurological findings in Canada. Pediatric Academic Societies Annual Meeting, Honolulu, Hawaii, May 2008. (Poster presentation)

The incidence of kernicterus in Canada. Annual Neonatal & Maternal-Fetal Medicine Research Day, Mount Sinai Hospital, Toronto, ON, April 2008. (Invited lecture)

# Methicillin-resistant *Staphylococcus aureus* in hospitalized children

September 2008 to August 2010

## Highlights 2008

- In the first four months of surveillance, the study confirmed 29 cases of hospitalized children with MRSA infections.
- MRSA infections in children were reported from all provinces and one territory.
- Of confirmed cases, 76% were community-acquired.

## Background

MRSA infections include hospital-associated methicillin-resistant *Staphylococcus aureus* (HA-MRSA) and community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infections. Compared to HA-MRSA, CA-MRSA is primarily acquired in the community setting and affects healthy ambulatory children and adults, causing skin and soft tissue infections, as well as severe disease and death, particularly necrotizing pneumonia, fasciitis, osteomyelitis and sepsis.

The majority of CA-MRSA infections are caused by two or three clones that are distinct in susceptibility to antimicrobials and genetic pattern from HA-MRSA. Most children with CA-MRSA have no recognized risk factors for infections. Pockets of CA-MRSA have been reported since the late 1980s amongst Aboriginal populations and in youth with risk factors such as drug use and incarceration.

In 2007, the Canadian Nosocomial Infection Surveillance Program (CNISP) determined that 21% of the patients (adults and children) admitted to participating hospitals with MRSA had CA-MRSA. We have limited information about the extent of disease, as CA-MRSA is reportable in five provinces and one territory.

## Objectives

- 1) Determine the annual number and proportion of children requiring hospitalization due to newly diagnosed MRSA infections across Canada
- 2) Describe the clinical spectrum of severe MRSA infections in children hospitalized in Canada
- 3) Identify potential risk factors for MRSA infections requiring hospitalization in Canadian children

## Case definition

Report all hospitalized children less than 18 years of age who have symptomatic MRSA infection, laboratory-confirmed from a clinical sample.

## Exclusion criteria

MRSA from a surveillance culture or as an incidental finding on culture

## Results

TABLE 23

Methicillin-resistant *Staphylococcus aureus* in hospitalized children cases from September 1 to December 31, 2008

Reported	Duplicates	Excluded	Pending	Confirmed
59	2	11	17	29

In the first four months of surveillance, 29 cases of MRSA infections were confirmed with 17 cases pending (Table 23). Females comprise a slightly higher percentage (55%) of cases than males and 79% of children are from urban areas. The mean age of reported cases is 5.8 years with a range of six weeks to 17 years. Interestingly, 18 (62%) children are 12 months of age or younger. The presentation of confirmed cases included 16 (41%) cases with skin or soft tissue infections, four (10%) with pneumonia, four (10%) with cervical adenitis, one each with mastoiditis, septic arthritis and osteomyelitis, while 12 (30%) had abscesses or other manifestations. Ten patients had more than one manifestation.

Vancomycin was started in four (14%) patients as initial therapy. The mean length of hospital stay was 17 days (range 3–90). Twenty-two patients (76%) had community-acquired infection, four (14%) were thought to have acquired infection in a health care facility and in three cases the source was unknown.



## Discussion/conclusion

Hospitalizations due to MRSA infections in children are occurring in most parts of Canada. As expected, this organism is primarily a community-acquired infection, which in these cases, has resulted in illness of sufficient severity to require hospitalization. Most of the children are young and as such, risk factors such as childcare or number of persons in a household may be important factors. A minority of children were treated initially with vancomycin indicating either low index of suspicion for MRSA or clinical situations that would warrant other initial therapy.

This report is preliminary and represents only the first four months of surveillance. Data on prevalence of known risk factors, associated infections and infection control precautions will be analyzed as the study continues. These data are important and are needed to develop preventative strategies.

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# Severe combined immunodeficiency

April 2004 to March 2010

## Highlights 2008

- In 2008, two cases of SCID were confirmed, diagnosed within 1.5 months of life.
- Earlier diagnosis carries a better prognosis as bone marrow transplantation can be performed before the appearance of overwhelming infections.
- Throughout the study, three cases have been confirmed in Aboriginal children.

## Background

Severe combined immunodeficiency (SCID) is a serious, life-threatening condition with high morbidity and mortality. As part of the strategy to reduce the incidence and severity of tuberculosis (TB) in children living on reserves with a high incidence of TB, the First Nations and Inuit Health Branch (FNIHB) of Health Canada has recommended the use of the live, attenuated BCG (bacille Calmette-Guérin) vaccine for newborns. However, concerns regarding both the efficacy and the safety of this vaccine have prompted FNIHB to reconsider this recommendation. Six cases of disseminated BCG infection in First Nations and Inuit children were reported between 1993 and 2002. All six children died. Four 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 Aboriginal children in regions 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 2.43 in 100,000 live births and in the United States Navajo population at 52 in 100,000 live births. Until this study, no Canadian incidence data for SCID was available.

## Objectives

- 1) Estimate the incidence of SCID in Canada
- 2) Estimate the incidence of SCID in Aboriginal children in Canada
- 3) Describe the basic demographics, clinical features and outcomes of SCID in Canada

## Case definition

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

- Absolute lymphocyte count of less than 3,000/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

TABLE 24

Severe combined immunodeficiency cases in 2008

Reported	Duplicates	Excluded	Pending	Confirmed
8	4	0	2	2

So far, two cases of SCID were confirmed in 2008; two other cases are pending, awaiting detailed case reports and/or further immunological data. Both confirmed cases were born in Canada; one male, one female. Neither reported a family history of immunodeficiency. The clinical features for both cases included diarrhea, rash, abscess, lymphadenopathy, *Pneumocystis carinii* pneumonia and failure to thrive. One case was diagnosed with an IPEX syndrome (Immunodysregulation polyendocrinopathy enteropathy X-linked syndrome) due to a FoxP3 mutation. The other case is awaiting more immunological data in order to finalize the specific type.

Fewer cases were reported in 2008 (n=8) than in 2007 (n=22) and 2006 (n=12). Only two cases were confirmed this year compared to eight last year and five in 2006. To date, three cases involving Aboriginal children have been confirmed. The appearance of cases in Aboriginal children will help in estimating the SCID incidence in this ethnic group, which is the second objective of the study. The confirmed cases in 2008 and 2007 were diagnosed at younger average ages than those reported in 2006 and 2005 (1.5 months and 3 months versus 5.8 months and 10 months). This trend is welcomed, as earlier diagnosis carries a better prognosis, and bone marrow transplantation

can be performed before the appearance of overwhelming infections.

## Conclusion

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 an average of five confirmed cases annually, the study results are 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.

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# Survey Questions

## Assessing CPSP surveillance methodology for ADR reporting

January 2008

A survey was conducted in December 2007 and January 2008, to assess the value of the CPSP in supporting increased recognition and reporting of serious and life-threatening adverse drug reactions (ADRs). Information was gathered on the ability of the CPSP to overcome the documented barriers to reporting associated with passive surveillance and the effectiveness of collaborative models in improving ADR reporting.

Information was collected via phone interviews, online questionnaire and mailed questionnaire. Phone interviews were conducted with eight Canadian Paediatric Society Board members. Over 700 survey responses were received, representing an approximate response rate of 28%.

Results clearly indicated that the CPSP has been instrumental in building and maintaining a culture of reporting amongst its members. It has simplified the reporting process and increased the likelihood of ADR reporting. Almost all (90%) respondents reported that they participate in the CPSP on a monthly basis, confirming the success of the program and highlighting the benefits of working with a national active surveillance program that promotes ongoing involvement and commitment of front-line members. When asked if serious and life-threatening ADRs were rare in children, 68% responded yes and 24% of respondents indicated that they had reported such an event during the study period.

Heavy workload, fear of legal liability and concerns with patient confidentiality are among the documented barriers associated with passive reporting systems. When asked about the barriers that impact the reporting of ADRs to the CPSP,

heavy workload (51%), time to complete the detailed questionnaire (39%) and difficulty in determining whether the problem is associated with a drug versus a disease (53%) were identified as significant barriers. Comments provided suggested that even a simple questionnaire represents an increased workload and that defining priorities for reporting would help manage workload issues as would electronic reporting. Concerns about legal liability and fear of breaching patient confidentiality were not seen as barriers to the reporting of ADRs to the CPSP. This most likely reflects the awareness of CPSP participants that every study undergoes approval by an independent Canadian research ethics board and that the program is committed to the rights of individual privacy and professional confidentiality.

Meaningful and targeted feedback is a critical measure of value and instrumental in building motivation and buy-in with active surveillance. All reporters, regardless of the reporting program, are looking for meaningful feedback with information targeted to specific areas or issues having the most impact on building buy-in and support. Greater feedback (61%), Tips of the Month (60%), increased training (61%) and a simplified questionnaire (53%) were all seen as solutions to support increased reporting by CPSP participants.

In order to improve paediatric drug safety, different types of partnerships are needed to better understand and accommodate the needs of physicians practising across a variety of settings. However, in trying to increase reporting, we may be creating under-reporting due to confusion. Competing interests must be minimized and synergies maximized. This evaluative survey has documented that collaboration with a national specialty active surveillance program is a very effective way to promote awareness and buy-in of participants to the ADR reporting process.

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## Paediatric pre-travel care

**February 2008**

Over 6.2 million Canadians travelled internationally in 2005 with less than 10% seeking pre-travel advice. In addition, the destinations travellers are visiting are expanding beyond North America and European Union countries to include more exotic travel in Latin America and Asia. With timely pre-travel health advice, a significant proportion of diseases presenting post-travel can be prevented.

Information obtained by paediatricians during a pre-travel visit should include details on the destination, planned activities, and type of accommodations, as well as the patient's medical history, including vaccinations. In addition to assessing the need for additional vaccines, the paediatrician has an opportunity to review general preventative measures.

The purpose of this study was to better understand the pre-travel care provided by paediatricians in Canada, using a one-time CPSP survey. The paediatric pre-travel care survey was sent to 2,451 CPSP participants and 650 responses were received (27%). Among respondents, nearly 70% reported having referred patients for pre-travel care in the past 12 months. The referrals were primarily to travel health clinics (50%), followed by public health units (17%) and infectious disease specialists (6%). Of the 452 paediatricians who made referrals, 64% also provided pre-travel advice to their patients. Paediatricians, who described their practice as primary care, consultative general paediatrics, or a combination of both, accounted for 67% of referrals and 74% of pre-travel care reports. The care was provided most commonly in a community-based setting (68%). The most frequent travel destinations reported were Latin America and the Caribbean (67%), followed by Asia (20%) and Africa (5%).

This survey highlights the important role health care providers currently play in identifying and

caring for high-risk travellers. Ongoing support to paediatricians for this important preventative role is important.

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## Renal stones and/or unexplained acute renal failure in infants

**October 2008**

Over the past year, an outbreak of renal stones and/or acute renal failure in association with the consumption of melamine-contaminated powdered infant formula has occurred in very young children in China. Other dairy products made in China and exported to other countries, including Canada, have been found to also contain melamine and were recalled from the market. Infant formula manufactured in China is not approved for sale in Canada. Health Canada has confirmed with the four major manufacturers of infant formula sold in Canada that they do not use any milk ingredients that come from China. In light of international travel, adoption and immigration, and the presence of melamine-contaminated dairy products, the question of Canadian infants being affected required a rapid response.

The Public Health Agency of Canada (PHAC) undertook to determine if there were cases of renal illness in Canadian children that may have been caused by the milk formula contamination in China. PHAC made a request to the CPSP to conduct a one-time emergency survey on the issue. The CPSP initiated the survey adapted from, and in collaboration with, the New Zealand Paediatric Surveillance Unit within 10 days of the PHAC request. Results were available three weeks after the survey was initiated.



There were 1,153 survey respondents, among the 2,475 CPSP participants surveyed (42%). In the past 12 months, slightly less than 10% of paediatricians reported that parents had consulted them about possible milk-product contamination. A total of eight paediatricians have reported 12 cases of infants (less than one year of age) with renal stones and/or unexplained acute renal failure. There were no cases of melamine-associated renal diseases. Other associated factors included urinary tract infections, hydronephrosis, diuretic therapy, hyperparathyroidism and prematurity. Hypercalciuria was present in seven cases and hyperoxaluria in one case.

The melamine example has demonstrated the potential for PHAC and the Canadian Paediatric Society to work together through the CPSP to carry out national emergency surveillance of rare conditions quickly and inexpensively, in order to inform public health responses to disease management and prevention.

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## Travel-related illnesses in paediatrics

### August 2008

Each year, increasing numbers of Canadian children and youth travel internationally. Up to 75% of travellers may develop a travel-related illness, and children account for a disproportionate number of travel-related hospitalizations. However, there is very little data available regarding travel-related

illnesses among Canadian children. The purpose of the survey was to determine how frequently CPSP participants had seen paediatric patients with travel-related illnesses, where they had travelled, and what types of illnesses had been seen.

The one-time survey was sent to approximately 2,499 CPSP participants in August 2008. There were 629 respondents (25%), of whom 184 (29%) had seen patients with travel-related illnesses during the previous 12 months. Children who were travelling to visit friends and relatives (VFRs) were seen by 70% of the respondents while tourist travellers and immigrant travellers were seen by 46% of respondents. Half of the respondents had seen travel-related illnesses among travellers to Africa while 42% of the illnesses occurred among travellers to India. Travel to Mexico, the Caribbean, and South and Central America was also commonly associated with travel-related illnesses. The most commonly seen travel-related illnesses were diarrheal diseases requiring hospitalization (57% of respondents), enteric fever (35%), malaria (34%) and other parasitic infections (22%).

Preliminary results of this survey were published as a CPSP Highlights in the March 2009 issue of *Paediatrics & Child Health*. Almost one-third of survey respondents see patients with travel-related illnesses. This emphasizes the need to obtain a detailed travel history. In addition, the majority of travel-related illnesses were seen among paediatric VFRs, which highlights the importance of discussing upcoming travel with families who are likely to visit friends and relatives in their countries of origin and providing or recommending pre-travel health advice for these patients. A CPSP surveillance study examining travel-related illnesses in paediatric travellers who visit friends and relatives abroad started in March 2009 to provide more detailed information about the illnesses experienced by this very at-risk group of travellers.

### Principal investigator

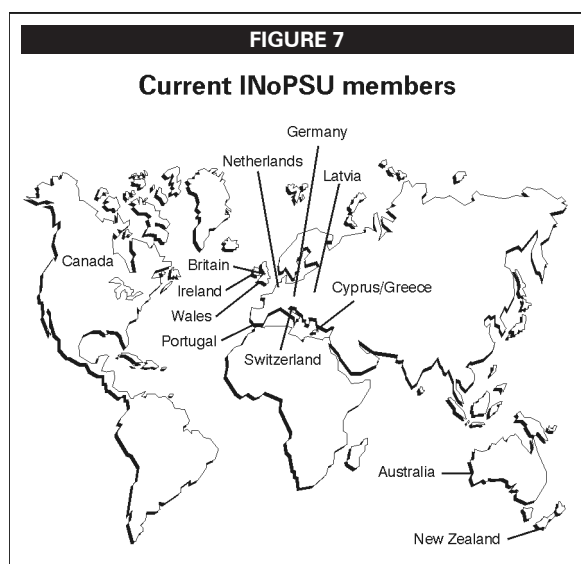
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# International Developments

## 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, there are 12 national paediatric surveillance units worldwide that are full members of INoPSU: Australia, Britain, Canada, Germany, Cyprus/Greece, Ireland, Latvia, Netherlands, New Zealand, Portugal, Switzerland, and Wales. The British Ophthalmological Surveillance Unit is an associate member.

The network remains active. In 2008, the fifth INoPSU conference took place in Munich, Germany. Daniel Virella, from the Portuguese Paediatric Surveillance Unit (PPSU), is the new convener and the British Paediatric Surveillance Unit (BPSU) continues to host the secretariat. Each national member agreed to update its study

data to ease searching by researchers who would be interested in conducting simultaneous studies in their home countries. Preparations are well underway for the sixth INoPSU conference, which will take place in 2010 (location to be finalized).

Further information on all national paediatric surveillance units can be obtained from the INoPSU website at [www.inopsu.com](http://www.inopsu.com). For the latest e-newsletter, visit [www.inopsu.com/publications/E-newsletter.html](http://www.inopsu.com/publications/E-newsletter.html).

## Highlights from international collaboration

### The Royal Australasian College of Physicians Congress, May 11–15, Adelaide

In May 2008, the CPSP participated in the Paediatrics and Child Health Scientific Meeting of the Royal Australasian College of Physicians Congress with the oral presentation, “Impacts of the International Network of Paediatric Surveillance Units.” The CPSP also chaired the Australian Paediatric Surveillance Unit (APSU) breakout session, “Congenital infections and vaccine preventable diseases.” Many challenging questions were discussed.

### The German Pediatric Society’s Annual Conference and the 5<sup>th</sup> INoPSU Meeting, September 11–14, Munich

In September 2008, the CPSP participated in the surveillance half-day at the German Pediatric Society’s annual conference with the oral presentation, “Impacts of the International Network of Paediatric Surveillance Units.” The INoPSU business meeting gathered most of the national paediatric surveillance units. Surveillance theme papers were presented and specific collaborative objectives were agreed upon.

TABLE 25

**Studies under surveillance  
by national paediatric surveillance units in 2008**

Study	National Paediatric Study Surveillance Units
Acute encephalitis/encephalomyelitis	PPSU
Acute flaccid paralysis	CPSP, NZPSU, SPSU
Acute post streptococcal glomerulonephritis	NZPSU
Acute rheumatic fever	SPSU
Adolescent pregnancy	LPSU
Adrenal insufficiency	IPSU
Adverse drug reactions – serious and life threatening	CPSP, NZPSU
Alcohol intoxication	NSCK
Anaphylaxis (immunization)	BPSU, ESPED, SPSU
Bleeding complications after tonsillectomy/adenoidectomy	ESPED
Bulimic eating disorders	CPSP
Cerebral palsy among five-year-olds	PPSU
Chronic fatigue syndrome	NSCK
Congenital adrenal hyperplasia	BPSU
Congenital cytomegalovirus infection	CPSP, PPSU
Congenital myotonic dystrophy	CPSP
Congenital renal or urological defects	NSCK
Congenital rubella syndrome	APSU, BPSU, NZPSU, SPSU
Congenital toxoplasmosis	CGPSU, PPSU
Conversion disorder	BPSU
Craniosynostosis	WPSU
Cystic fibrosis	NSCK
Diabetes mellitus	CPSP, LPSU, PPSU
Epistaxis in infancy	WPSU
Extended-spectrum $\beta$ -lactamase-producing enteric Gram-negative bacilli	SPSU
Fetal alcohol syndrome	NSCK
Feto-maternal alloimmune thrombocytopenia	BPSU
Gallstones	WPSU
Genital herpes under 11 years	BPSU
Group B streptococcal sepsis	APSU, PPSU
Head injuries secondary to suspected child maltreatment (abuse or neglect)	CPSP
Hemoglobinopathy	NSCK
Hemolytic uremic syndrome	CGPSU, NZPSU, PPSU, SPSU

Hepatitis C virus infection	APSU
HIV/AIDS (perinatal HIV exposure)	BPSU, NZPSU
Hyperbilirubinemia	NSCK, SPSU
Idiopathic intracranial hypertension (pseudotumor cerebri)	BPSU, ESPED
Inborn errors of metabolism	NZPSU
Influenza	APSU, ESPED
Interrupted pregnancy in adolescents	LPSU
Intussusception	BPSU
Juvenile idiopathic arthritis	CPSP
Juvenile myoclonic epilepsy	WPSU
Kawasaki disease	NSCK, PPSU
Kernicterus	CPSP
Leukemia	LPSU, NSCK
Long-term ventilation	WPSU
Lymphoma: Hodgkin's, non-Hodgkin's	LPSU
Medium-chain acyl-CoA dehydrogenase deficiency	BPSU, CPSP
Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA)	CPSP
Multiple sclerosis/ADEM	NSCK
Neonatal herpes simplex virus infection	SPSU
Osteitis, non-bacterial	ESPED
Pertussis	SPSU
Progressive intellectual and neurological deterioration (PIND)	BPSU
Severe asthma	ESPED, NSCK
Severe combined immunodeficiency	CPSP
Sudden unexpected early postnatal collapse	BPSU
Toxic shock syndrome	BPSU
Transfusion-related acute lung injury	CPSP
Varicella (neonatal, congenital, and complications)	IPSU, PPSU
Vitamin D deficiency rickets	WPSU
Vitamin K deficiency bleeding/HDNB	BPSU, NZPSU, SPSU
Walker injuries	PPSU

**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 2008, the APSU launched the book, *APSU: Celebrating 15 years of Surveillance 1993–2007*. The APSU also called for a national response to the significant impacts of rare childhood diseases in Australia and conducted an active hospital-based surveillance similar to the IMPACT system in Canada. This paediatric active enhanced diseases surveillance (PAEDS) looked at influenza complications in four paediatric hospitals in four states of Australia.

### Britain

In 2008, the BPSU secured a grant extension to the spring of 2012 from the Department of Health (DH). In conjunction with the DH policy unit, a work program was drawn up which will reflect the research priorities within the DH and the needs of those who wish to use the BPSU.

An internal evaluation was also conducted using the Centers for Disease Control and Prevention Atlanta guidelines on assessing surveillance systems. Feedback was positive and the system was found to be both useful and valued by paediatricians, with 84% considering the surveillance of rare paediatric diseases to be important and 43% stating that they had changed their clinical practice following the outcome of BPSU studies.

### Germany

After the completion of a ten-year study (1998–2007) on invasive *Haemophilus influenzae* infections (all types), the German Paediatric Surveillance Unit saw the publication of an article by A Milde-Busch et al. in the *European Journal of Public Health* entitled, “Surveillance for rare infectious diseases: Is

one passive data source enough for *Haemophilus influenzae*?”

### Netherlands

The past year has seen the Netherlands Paediatric Surveillance Unit study on alcohol intoxication in children highlighted in the press with 337 children admitted (13% more than in 2007). The mean age was 15 years and the youngest 10 years of age. Almost half (48%) were boys. The mean blood alcohol level was 1.9 promille, the equivalent of about 10 glasses of alcohol. To address this problem, five polyclinics were started across the country.

### New Zealand

The New Zealand Paediatric Surveillance unit successfully undertook rapid national surveillance to explore the possibility of melamine-associated renal stones in infants. A new study on proven neonatal bacterial or fungal infection in the first week of life has been approved to start in 2009.

### Portugal

Over the next couple of years, new INoPSU convenor Daniel Virella from the Portuguese Paediatric Surveillance Unit wishes to strengthen and raise the profile of the network, including activities and output. He also encouraged closer



INoPSU conference, Munich, Germany, September 2008

associations between national units undertaking simultaneous studies. One of his goals is for each unit to advocate for a national plan on rare diseases at the government level and to encourage further epidemiological research to advance knowledge in this field.

### **Switzerland**

In the past year, the Swiss Paediatric Surveillance Unit completed a seven-year study on neural tube defects (NTDs) and identified 140 cases. Of these, 68 cases (48%) were born alive and included 58 meningoceles, nine encephaloceles and one anencephaly. A Poretti et al. published an article in the *Swiss Medical Weekly* entitled “Neural tube defects in Switzerland from 2001 to 2007: Are periconceptual folic acid recommendations being

followed?” NTDs remain a frequent problem in Switzerland, although correct periconceptual folic acid supplementation is known to be effective in reducing the prevalence of NTDs. Consequently, only a public health policy that includes folic acid fortification of food is likely to result in significant prevention of NTDs.

### **Wales**

Over the past year, the Welsh Paediatric Surveillance Unit (WPSU) has successfully changed its reporting system from a card-based to a chiefly electronic means of reporting cases, with virtually no change in the response rate. Reports are submitted to the WPSU office very quickly, with more than two-thirds arriving within two days of the “electronic cards” going out.



## RESEARCH OPPORTUNITIES

# Call for New Studies

### Wanted

Investigators to initiate new CPSP studies

### The program

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

### Track record

- 80% response from more than 2,500 paediatricians
- 94% data completion rate

### Study ideas

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

Bipolar disorder	Hypernatremia or hyponatremia
Brachial plexus injury	Hyperthyroidism
Bronchiectasis	Idiopathic intracranial hypertension
Celiac disease	Imported malaria
Childhood tuberculosis	Life-threatening events/unexplained deaths (first day of life)
Circumcision complications	Neonatal listeria infections
Congenital adrenal hyperplasia	Perinatal HIV infections
Conversion disorder	Rett syndrome
Fatal and near-fatal asthma	Shingles

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  
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