



CPSP

CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM



2009 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.



From a Research Idea to Action

Child safety no longer takes a back seat



Background

- Motor vehicle crashes are the leading cause of death and disability in children.
- Seat belts reduce fatalities and the severity of injuries.
- Guidelines on age-appropriate restraints have emerged.
- “Seat-belt syndrome” is a new association of injuries with improper use of seat belts, commonly referred to as “lap-belt syndrome.”



Question to answer

In Canada, how many cases of lap-belt syndrome occur in children each year?



Methodology

- CPSP study from September 2003 to August 2005
- Initial report form and detailed questionnaire



Results

- 28 cases of lap-belt syndrome were confirmed during the two-year study.
- There was a high prevalence of spinal fracture (43%) and permanent spinal cord lesion (24%).
- Although 12 children were less than eight years old, only one was restrained in a booster seat.



Analysis and interpretation

- Seat belts save lives; however, if used incorrectly they can cause serious abdominal and lumbar spine injuries.
- Aggressive education efforts are urgently needed to ensure adequate restraint in motor vehicles.



Publication and dissemination

Professional



Advocacy



Public



Advocacy in action

- In 2005, few provinces and territories had any booster seat legislation for children aged four to eight.
- By 2009, with continued advocacy and education efforts in concert with other groups, six provinces have excellent booster seat legislation for this age group.

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Acknowledgements



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

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

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.

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 maintain and expand the program.

We gratefully acknowledge the financial support received in 2009 from the Public Health Agency of Canada, Health Canada's Therapeutic Effectiveness and Policy Bureau, and the following non-governmental sources:

- Complementary and Alternative Research and Education Program, University of Alberta
- Histiocytosis Association of Canada
- St. Michael's Hospital Innovation Fund
- University of Manitoba
- William Singeris National Centre for Myotonic Dystrophy Research

Foreword

Federal Minister of Health

I am pleased to congratulate the Canadian Paediatric Society on another successful year of managing the Canadian Paediatric Surveillance Program (CPSP), and on its completion of this program's fourteenth annual report.

The CPSP gathers information from over 2,500 paediatricians and paediatric subspecialists every month to monitor rare diseases and conditions in Canada's children and youth. Monitoring is a complex and comprehensive undertaking, and is crucial to helping determine the burden of disease in children and to better understanding risk and protective factors. It also helps guide future health policies, both in Canada and internationally.

The contributions of paediatricians and other specialists are vital to the program's success. I commend the dedication and commitment of everyone involved.

The Government of Canada is proud to work with the Canadian Paediatric Society, its members, the provinces and territories, and other partners in providing a healthier future for Canadian children and youth.



The Honourable
Leona Aglukkaq

Chief Public Health Officer of Canada

As Chief Public Health Officer of Canada, I am very proud to accept the fourteenth annual report from the Canadian Paediatric Surveillance Program (CPSP). Once again, this program has demonstrated its capacity to be both a relevant and timely surveillance system.

When the 2009 influenza A H1N1 reached the pandemic level in Canada, the CPSP contributed to the federal government's response by working with Health Canada and the Public Health Agency of Canada to gather information about the possible adverse reactions occurring with the use of antiviral drugs in Canadian children and youth.

This collaboration was essential in ensuring quick and appropriate action on H1N1. I am grateful to the paediatricians who diligently completed and returned report forms every month. Without their contribution, the program would not be as successful as it is.

I would also like to thank the CPSP Steering Committee, the CPS staff and the Public Health Agency of Canada staff for their 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 an active collaborative network of paediatric surveillance in Canada to advance knowledge of rare diseases in children and youth.

As a community paediatrician, I appreciate the chance to participate in the Canadian Paediatric Surveillance Program, and know that my contribution is as important as that of my paediatric subspecialist colleague. All of us are committed to translating the research results to our patients and their families. We can also ensure that preventive and/or curative measures identified through surveillance will be disseminated promptly. Since paediatricians are present in all provinces and territories, an added advantage of being part of the CPSP is the possibility of using the findings to advocate at every governmental level for much needed changes.

Every paediatrician can make a difference in the life of a child with a rare disease. The monthly surveillance reports of all paediatricians and paediatric subspecialists help achieve that goal and are greatly appreciated.

As you can see, the CPSP is a well established and vigorous program. Thanks to every one of you for your important contribution.



Dr. Kenneth J.
Henderson

CPSP Chairman

As Chair of the Canadian Paediatric Surveillance Program Steering Committee, I am pleased to report that the CPSP remains as productive, informative and relevant as ever, thanks to the excellent work of everyone involved and mutual support and collaboration between the Canadian Paediatric Society and the Public Health Agency of Canada.

Over the past year, the Steering Committee has reviewed proposals for 13 studies and four surveys. One of the surveys demonstrated the ability of the CPSP to respond rapidly to a public health emergency, namely the use of antiviral drugs during the H1N1 influenza epidemic. Another survey evaluated the readiness of the participants for Web-based reporting as an evolving surveillance methodology. I encourage you to read the survey results summary on page 47.

CPSP studies are currently collecting important epidemiological data on a broad range of high-impact paediatric conditions, including bulimic eating disorders (page 22), severe iron-deficiency anemia in infants and young children (page 41), and travel-related illnesses in paediatric travellers who visit friends and relatives abroad (page 43), to name a few.

Surveillance research draws its strength from the commitment of the participating paediatric community. Every report counts. My thanks to all of you for making the important work of the CPSP possible. I am looking forward to many more years of national paediatric epidemiological research.



Dr. Lonnie
Zwaigenbaum

CPSP Steering Committee

Dr. Lonnie Zwaigenbaum (Chair)	Canadian Paediatric Society
Dr. Denis Daneman	Paediatric Chairs of Canada
Ms. Marie Adèle Davis	Canadian Paediatric Society
Dr. Kimberly Dow	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
Dr. Dorothy Moore	IMPACT (Immunization Monitoring Program ACTive) (Liaison)
Mr. Paul Muirhead	Consultant
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. Tom Wong	Infectious Disease and Emergency Preparedness Branch, Public Health Agency of Canada
Dr. Sandra Woods	Canadian Paediatric Society



In March 2009, **Dr. Wendy Vaudry** completed her term as the IMPACT liaison on the CPSP Steering Committee. We sincerely thank Wendy for her work over the past eight years and wish her the best in her role as an IMPACT co-principal investigator.

CPSP Working Group

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

Publications 2005-2009



Published papers related to studies

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

Acquired demyelinating syndromes of the CNS

Incidence of acquired demyelination of the CNS in Canadian children. Banwell B, Kennedy J, Sadvnick D, Arnold DL, Magalhaes S, et al. *Neurology* 2009; 72: 232-9

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

Complementary and alternative medicine

Adverse events associated with paediatric use of complementary and alternative medicine: Results of a Canadian Paediatric Surveillance Program survey. Vohra S, Brulotte J, Le C, Charrois T, Laeque H. *Paediatr Child Health* 2009; 14(6): 385-7

Congenital myotonic dystrophy

Patient registries and trial readiness in myotonic dystrophy: TREAT-NMD/Marigold International Workshop Report. Campbell C. Additional outcome measures for childhood and congenital DM1. Thompson R, Schoser B, Blonsky K, Lochmuller H. *Neuromuscul Disord* 2009; 19: 860-6.

Haemolytic uraemic syndrome

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

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

Lap-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

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, Zurynski Y, Pereira RR, Preece M, Lynn R, von Kries R, Zimmerman H, Dickson NP, Virella D. *Arch Dis Child* 2007; 92: 527-33

Vitamin D deficiency rickets

Vitamin D-deficiency rickets among children in Canada. Ward LM, Gaboury I, Ladhani M, Zlotkin S. *CMAJ* 2007; 177(2): 161-6

Highlights published in 2009 in *Paediatrics & Child Health*

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

Respiratory distress and the flu: What should a physician know? *Paediatr Child Health* 2009; 14(9): 571-2

Public health impacts of the International Network of Paediatric Surveillance Units. *Paediatr Child Health* 2009; 14(8): 499-500

Developmental regression: Always a worrying signal. *Paediatr Child Health* 2009; 14(7): 431

Children and spinal manipulation therapy: Ask your patients about all the therapies they seek. *Paediatr Child Health* 2009; 14(6): 388

Can active surveillance provide a rapid response to an emerging child health issue? The melamine example. *Paediatr Child Health* 2009; 14(5): 285-6

Is melamine contamination an issue in Canada? *Paediatr Child Health* 2009; 14(4): 218

Canadian children who travel abroad: What are the risks? *Paediatr Child Health* 2009; 14(3): 160, 176

Know before you go: Safe travels. *Paediatr Child Health* 2009; 14(2): 123

MRSA: New twists from an old pathogen. *Paediatr Child Health* 2009; 14(1): 39,48

Presentations in 2009

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

National

Child maltreatment

Head injury secondary to suspected child maltreatment in Canada: a 3-year surveillance study. Ward M. Children's Hospital of Eastern Ontario Research Day, Ottawa, in October (oral)

Recent headlines in the news: Controversies in inflicted head trauma. Shouldice M, Ward M. Canadian Paediatric Society Annual Conference, Ottawa, in June (oral)

The extent and nature of head injury secondary to child maltreatment in Canada: A 3-year surveillance study. Bennett S, Ward M, Fortin G, Plint A, Clifford T, King J, Mackay M. Canadian Paediatric Society Annual Conference, Ottawa, in June (poster)

Kernicterus

The incidence of kernicterus in Canada 2007-2009. Sgro M, Campbell DM, Shah V, Fallah S. Canadian Paediatric Society Annual Conference, Ottawa, in June (poster)

A bili for every baby: Easy to say, hard to do. Campbell D, Jangaard K, Sgro M. Canadian Paediatric Society Annual Conference, Ottawa, in June (oral)

The incidence of kernicterus in Canada 2007-2009. Sgro M, Campbell D, Shah V, Fallah S, Jacob A. Annual Neonatal & Maternal-Fetal Medicine Research Day, Mount Sinai Hospital, Toronto, in April (poster)

Medium chain acyl-coenzyme A dehydrogenase deficiency

The expanding spectrum of medium chain acyl-coenzyme A dehydrogenase deficiency (MCADD)

from trait to lethality: MCADD experience using the Canadian Paediatric Surveillance Program. Prasad C, Speechley KN, Dyack S, Rupar CA, Chakraborty P, Kronick JB. Canadian Paediatric Society Annual Conference, Ottawa, in June (poster)

Surveillance – General

La surveillance pédiatrique : « Un atout pour la recherche ». Grenier D, Laffin Thibodeau M. Grand Rounds, Centre hospitalier de l'Université Laval, Quebec City, in February (oral)

Transfusion-related acute lung injury (TRALI)

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

Travel-related illnesses

Travel-related illnesses and conditions in paediatrics. Grenier D, Ugnat AM, Davis MA, Skinner R, Laffin Thibodeau M. Canadian Paediatric Society Annual Conference, Ottawa, in June (poster)

International

Congenital myotonic dystrophy

Congenital myotonic dystrophy: Canadian surveillance and cohort study. Taranik R, Campbell C. International Myotonic Dystrophy Consortium Meeting, Würzburg, in September (oral)

Motor outcome measures in congenital and childhood DM1. Ho A, Campbell C. International Myotonic Dystrophy Consortium Meeting, Würzburg, in September (poster)

Quality of life and family impact of congenital and childhood DM1. Ho A, Bax K, Campbell C. International Myotonic Dystrophy Consortium Meeting, Würzburg, in September (poster)

Kernicterus

The incidence of kernicterus in Canada 2007-2009. Sgro M, Campbell DM, Shah V, Fallah S. Pediatric Academic Societies Annual Meeting, Baltimore, in May (poster)

Surveillance – General

Active neonatal disease research through surveillance: The Canadian experience. Grenier D, Sgro M, Prasad C. European Society for Paediatric Research Annual Meeting, Hamburg, in October (poster)

The International Paediatric Surveillance Network – Research in action. Grenier D, Ugnat AM, Laffin Thibodeau M, Lynn R. Medical & Nursing Annual Congress of the European Society of Paediatric and Neonatal Intensive Care, Verona, in June (poster)

Indigenous health research through surveillance. Grenier D, Ugnat AM, Davis MA, Laffin Thibodeau M. International Meeting on Indigenous Child Health: Many Voices Into One Song, Albuquerque, in March (poster)

Travel-related illnesses

Travel-related illnesses in Canadian children (TRIP study). Crockett M, Hui C, Kuhn S, Ford-Jones L, Keystone J. Infectious Diseases Society of America Annual Meeting, Philadelphia, in October (poster)



Surveillance at Work

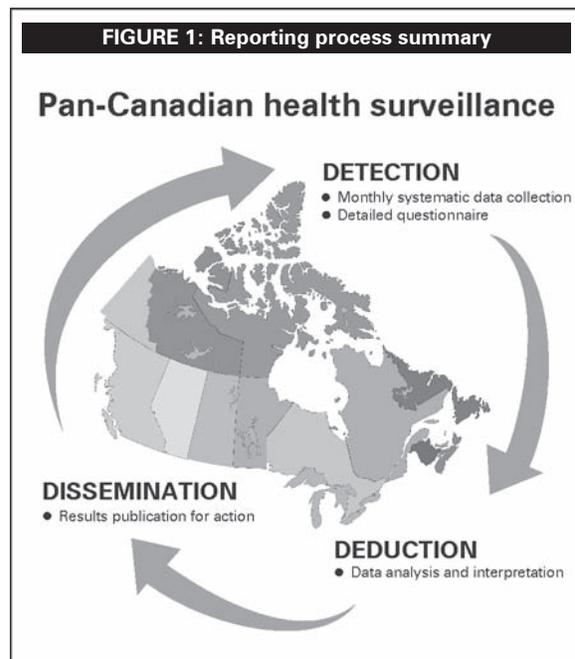
Overview

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, through the International Network of Paediatric Surveillance Units (INoPSU), 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 2009

Provinces/territories	Reporting rates (%)	Number of participants
Alberta (AB)	78	303
British Columbia (BC)	78	267
Manitoba (MB)	84	111
New Brunswick (NB)	79	28
Newfoundland and Labrador (NL)	85	51
Nova Scotia (NS)	87	98
Northwest Territories (NT)	100	2
Nunavut (NU)	100	1
Ontario (ON)	82	969
Prince Edward Island (PE)	99	7
Quebec (QC)	80	607
Saskatchewan (SK)	74	58
Yukon (YT)	100	1
Canada	81	2,503

TABLE 2
2009 detailed questionnaire completion rates
as of May 1, 2010

Studies/conditions	Reported cases*	Pending	% Completion rate
Acute flaccid paralysis	72	14	81
Adverse drug reactions – serious and life-threatening	60	14	77
Bulimic eating disorders	89	17	81
Congenital myotonic dystrophy	13	2	85
Juvenile idiopathic arthritis	287	7	98
Kernicterus	5	2	60
Langerhans cell histiocytosis	9	3	67
Methicillin-resistant <i>Staphylococcus aureus</i> in hospitalized children	107	20	81
Serious adverse events associated with paediatric complementary and alternative medicine	7	1	86
Severe combined immunodeficiency	9	1	89
Severe iron-deficiency anemia in infants and young children	22	8	64
Travel-related illnesses in paediatric travellers who visit friends and relatives abroad	38	5	87
Total number of cases (all studies)	718	94	87

* 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

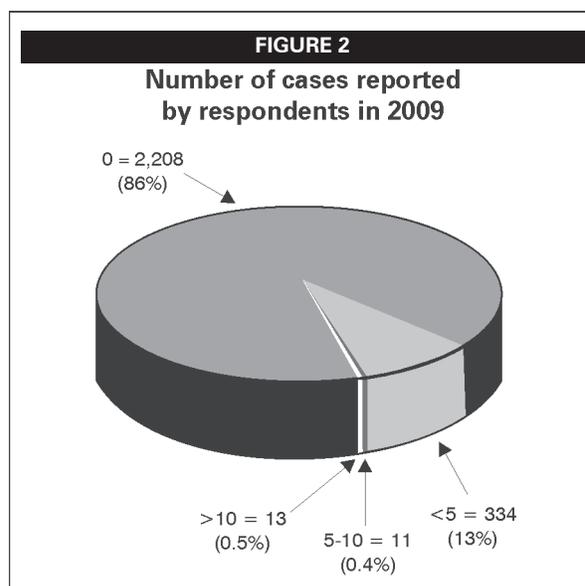
reported is mailed quarterly to all participants to keep them informed of progress. The CPSP is encouraged by the 81% national reporting rate (Table 1) and the 87% response rate for completion of detailed questionnaires (see Table 2 for study breakdown).

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 2009, the majority of participants (86%) had ‘nil’ cases to report. The importance of zero reporting must be re-emphasized. Figure 2 illustrates the number of cases reported by respondents in 2009. As studies come and go, the workload shifts to different subspecialties. Through the years, studies with national collaborative networks have been very successful. The 2009 studies with the most reports were Juvenile idiopathic arthritis, Methicillin-resistant *Staphylococcus aureus* in hospitalized children, 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, letters of appreciation were sent to participants who completed the initial reporting forms for all months in 2009 and/or returned one or more detailed questionnaires. In addition, Drs. Lynn Patricia Straatman (British Columbia) and Manuel Saul Greenberg (Ontario) were selected in this year's early-bird draw, each winning a dinner for two. The lucky winners of the year-end draws for a complimentary registration to attend the June 2010 CPS Annual Conference in Vancouver, British Columbia, were Dr. Fionnuala O'Kelly (Ontario), who responded for all months in 2009, and Dr. Miriam Weinstein (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 2,503 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 87% on detailed questionnaires (Table 2). The CPSP offers an opportunity for international collaboration with other paediatric surveillance units worldwide and a chance to make a difference in the health and well-being of Canadian children and youth.

Individual researchers are encouraged to submit proposals for new studies that meet the Criteria considered for inclusion of studies outlined in Table 3 and follow the Format for submission detailed in Table 4. The Steering Committee reviews submissions at its spring and fall meetings, giving preference to studies that have either strong scientific and public health importance or 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 Web site at www.cps.ca/cpsp or contact the CPSP senior coordinator at cpsp@cps.ca.

One-time survey questions

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

Results of the 2009 one-time survey questions are found on pages 46–8.

TABLE 3

Criteria considered for inclusion of studies

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

TABLE 4

Format for submission

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

Glossary of terms for tables of cases in each study results

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

Studies timeline

TABLE 5
CPSP studies timeline (by end date)

Study	Start date	End date	Total confirmed cases to December 31, 2009
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	846
Kernicterus	January 2007	December 2009	22
Congenital myotonic dystrophy	March 2005	February 2010	37
Bulimic eating disorders	March 2008	February 2010	125
Severe combined immunodeficiency	April 2004	March 2010	35
Methicillin-resistant <i>Staphylococcus aureus</i> in hospitalized children	September 2008	August 2010	118
Acute flaccid paralysis	January 1996	December 2010	619
Adverse drug reactions – serious and life-threatening	January 2004	December 2010	237
Serious adverse events associated with paediatric complementary and alternative medicine	January 2009	December 2010	4
Travel-related illnesses in paediatric travellers who visit friends and relatives abroad	March 2009	February 2011	30
Langerhans cell histiocytosis	July 2009	June 2011	5
Severe iron-deficiency anemia in infants and young children	October 2009	September 2011	9

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
Congenital cytomegalovirus infection – Post-study survey	February 2009
Web-based reporting	July 2009
Paediatric antiviral drug use and potential adverse reactions	November 2009

CPSP Principal Investigators



Surveillance studies in 2009



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Acute flaccid paralysis



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Adverse drug reactions – serious and life-threatening



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Methicillin-resistant *Staphylococcus aureus* in hospitalized children



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Serious adverse events associated with paediatric complementary and alternative medicine



Dr. RoseMarie Ramsingh
Severe combined immunodeficiency



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Severe iron-deficiency anemia in infants and young children



Dr. Maryanne Crockett
Travel-related illnesses in paediatric travellers who visit friends and relatives abroad

Surveillance Studies in 2009



Acute flaccid paralysis

January 1996 to December 2010

Highlights 2009

- Canada met the WHO's non-polio AFP rate of at least one case for every 100,000 children less than 15 years of age; a target that has not been met since 2000.
- Vigilant surveillance is essential since there is ongoing transmission of wild poliovirus in endemic countries with some previously polio-free countries experiencing reintroduction of poliovirus.
- Neurological investigations (MRI, EEG, etc.) occur in greater than 85% of all AFP cases.
- Guillain-Barré syndrome continues to be the most frequent diagnosis for AFP in Canada.

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 2009, endemic circulation of wild poliovirus continued in four countries: Afghanistan, India, Nigeria and Pakistan. There were 1,596 cases of wild poliovirus reported from a total of 23 countries worldwide as compared with 1,618 cases during 2008 (Global Polio Eradication Initiative). 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 international 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., postictal weakness) does not meet the case definition.

Results

There were 79 notifications of AFP through the CPSP to the Public Health Agency of Canada with onset in 2009, which included 57 confirmed cases (Table 7). Case ascertainment for all confirmed cases in 2009 occurred in equal proportions between IMPACT sites and the CPSP. In addition,

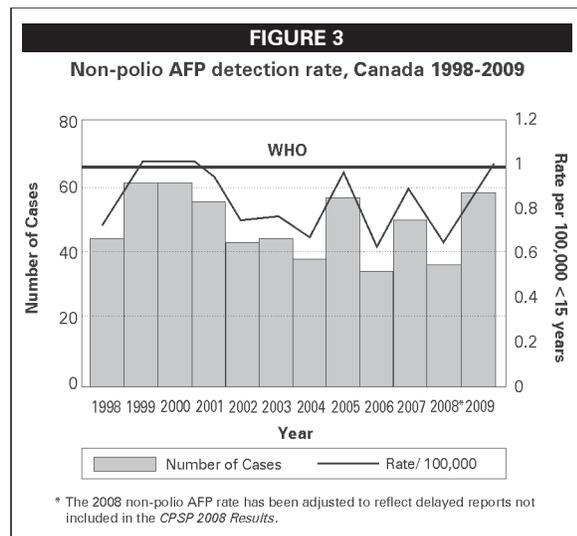


there was a higher proportion (58%) of confirmed cases reported from Ontario and Quebec. The remaining confirmed cases were reported from Western Canada (39%) and Eastern Canada (3%). As this study is ongoing, AFP delayed reporting occurs and the figures are adjusted accordingly once detailed case reports have been received.

TABLE 7
AFP cases in 2009

Reported	Duplicates	Excluded	Pending	Confirmed
79	2	6	14	57

Eight AFP reports were excluded: five based on age criteria, one based on diagnosis and two duplicates. The 57 confirmed cases in 2009 represent a non-polio AFP detection rate of 1/100,000 in children less than 15 years of age (Figure 3) which meets WHO's expected rate of 1/100,000 per year. As documented in previous years, Canada's annual AFP incidence rate has been artificially low due to delays in receiving detailed case report forms.



In 2009, AFP cases ranged in age from one month to 14 years (median 7 years, mean 7 years), and were fairly evenly distributed across the age groups. Similar to last year's results, the majority (60%) of AFP cases were reported in males as compared to females.

Documentation of age-appropriate polio immunization with inactivated poliovirus (IPV) vaccine remains incomplete; only five (9%) cases

had documented receipt, 17 (30%) were reported as "up-to-date" but with no accompanying details, and the remaining 35 (61%) included no information. Of note, vaccine uptake rates of IPV in Canada have been consistently high.

Investigation for polio virus, other enteroviruses or Campylobacter

Virological investigation included collection and testing of stool specimens for 27 cases (47%), cerebrospinal fluid (CSF) for 38 cases (67%) and throat swabs for 20 cases (35%). Where stool was collected, 67% had an adequate sample taken within 14 days from the onset of paralysis. In the remaining cases, stool collection was later, when the sensitivity of virus isolation is lower. In Canada, the proportion of adequate stool samples collected within 14 days of the onset of paralysis has been consistently below the WHO surveillance target of 80%. In 2009, the proportion was 32%; however, these proportions have fluctuated from a low of 30% in 1998 to a high of 54% in 2000. In 2009, there was no positive identification of polioviruses from any of the virological investigations. Testing was also conducted for *Campylobacter* in 18 (32%) cases and was not isolated in any of the samples.

Neurological investigations

In 2009, approximately 88% of cases underwent at least one type of neurological investigation (CSF examination, nerve conduction studies/electromyography (EMG), MRI/CT scan) with CSF exams used most frequently. Of these, approximately 58% had abnormal CSF chemistry results, 85% abnormal EMG and/or nerve conduction studies and 68% abnormal MRI or CT scans.

As observed in previous years, the majority of AFP cases (n=30, 53%) were GBS, two of which were Miller-Fisher variant. The remaining 27 diagnoses included acute disseminated encephalomyelitis (n=6), primary demyelinating disorders (n=15), infantile botulism (n=1) and other (n=5).

Hospitalization and outcome

All confirmed AFP cases reported in 2009 required hospitalization, with lengths of stay ranging from one to 120 days (median 11 days, mean 18 days). For two cases, the lengths of stay were unknown. Outcome at the time of the initial report was documented in

51 cases: six (12%) fully recovered, 35 (68%) partially recovered with residual weakness or paralysis, and 10 (20%) who had not fully recovered but were reported to be improving. There were no deaths. Only 25 cases (44%) had clinical status at 60 days reported, including eight cases who had fully recovered, eight with partial recovery, some residual weakness or paralysis and nine with outcomes pending. This remains below the 80% WHO recommended target for high-quality AFP surveillance but may be due to timing of report completion/submission.

Conclusion

A total of 57 AFP cases were confirmed in 2009, giving a national non-polio AFP detection rate of one case per 100,000 population in children less than 15 years of age, which meets WHO's quality assurance criteria. Previously, the recommended target had only been met twice (in 1999 and 2000) since AFP surveillance began in 1996. This achievement was the result of increased and timely reporting. Canada's consistently lower than expected AFP rates over the years 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: an increase in the proportion and timeliness of 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 (GPEI)

www.polioeradication.org

In 2009, while just over 1,596 cases of poliomyelitis were reported globally, only 78% of these occurred in the four countries where indigenous polio transmission is still occurring: Nigeria, India, Pakistan and Afghanistan. The remaining cases occurred in non-endemic countries; this serves as an important reminder of the possibility of importation, especially in countries that have been polio-free for many years. While polio eradication has faced some challenges, in 2009 the GPEI announced the use of a new bivalent oral polio vaccine (types 1 and 3) currently being used in all endemic countries, which demonstrates greater than 30% effectiveness over the trivalent oral polio vaccine.

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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Adverse drug reactions – serious and life-threatening

January 2004 to December 2010

Highlights 2009

- In 2009, the study confirmed 45 cases of suspected paediatric adverse drug reactions.
- Product groups most commonly associated with suspected adverse reactions were anticonvulsant, anti-infective and antineoplastic agents.

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, 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 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 radiopharmaceutical 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

TABLE 8

Serious and life-threatening ADR cases in 2009

Reported	Duplicate	Excluded	Pending	Confirmed
67	1	6	15	45

In 2009, 67 cases of suspected serious ADRs were reported and 45 were confirmed (Table 8). By comparison, 35 and 45 cases were confirmed in 2008 and 2007 respectively.

The confirmed suspected serious ADR reports included 26 males, 18 females and in one case the sex of the patient was not provided. Table 9

provides a comparison of the age distribution of cases for the past three years.

TABLE 9
Annual comparison of age distribution

	2009 (n=45)	2008 (n=35)	2007 (n=45)
Up to 5 years of age	12	15	9
6 to 12 years	13	9	16
13 to 17 years	20	11	18
Not reported	0	0	2

Forty-five cases were classified as serious (more than one reason for seriousness was given in 14 reports). Table 10 gives a comparison of the reasons for seriousness of the ADR reports for the past two years.

TABLE 10
Annual comparison of reasons for seriousness

	2009 (n=45)	2008 (n=35)
Death	1	3
Life-threatening	14	12
Hospitalization	28	21
Disability	1	0
Medically important condition*	21	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.

Information regarding patient outcome was provided for 39 of the 45 reports as follows: recovered (n=31); not yet recovered (n=6); recovered with sequelae (n=1); fatal outcome (n=1). The one fatal report involved a patient who received a five-day course of an investigational product, clofarabine, for the treatment of resistant relapsing acute lymphoblastic leukemia. Cytarabine was concomitantly given. The day following the last dose of clofarabine, the patient developed pulmonary edema, renal failure and hypotension and died 48 hours after completing clofarabine treatment.

All reports described reactions that were documented in standard drug reference sources for the health product except for three: (1) dystonic-like posturing of the arm, slurred speech and

vacant gaze associated with oral administration of prednisolone; (2) aggravation of pre-existing symptoms of obsessive-compulsive disorder with methylphenidate; (3) serotonin syndrome following co-administration of olanzapine and granisetron. 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, the Micromedex™ Drug Information System or the American Hospital Formulary Service™ (AHFS) Drug Information reference.

Suspected health products

Table 11 lists all health products suspected of causing ADRs in the 45 confirmed cases, sorted by the number of reports received per each individual product. In 40 reports, a single product was suspected of causing the reaction(s). Two suspect products were reported in five cases. The class of health products most frequently suspected was anticonvulsants (n=9), followed by anti-infective agents (n=8) and antineoplastic agents (n=6). These findings are similar to those observed in 2008 (with the exception that the most frequently involved class of products was anti-infectives).

TABLE 11
**Suspected or interacting health products (50)
in ADR reports (45) in 2009**

Suspected health product	# Reports
Carbamazepine	4 (n=4)
Amoxicillin, divalproex sodium, ibuprofen, immune globulin intravenous (human), infliximab, methylphenidate, minocycline	2 each (n=14)
Allergen extract, atomoxetine, azathioprine, cefotaxime, ceftriaxone, charcoal, cidofovir, clofarabine, cytarabine, daunorubicin, granisetron, isotretinoin, ketamine hydrochloride, ketorolac, lamotrigine, magnesium sulphate, methotrexate, metoclopropamide, morphine, nelarabine, olanzapine, oxcarbazepine, pegaspergase, phenytoin, prednisolone, propafenone, risperidone, sertraline, sulfamethoxazole-trimethoprim,* tramadol/acetaminophen*, vancomycin, voriconazole	1 each (n=32)

* Combination products containing two active ingredients

Conclusion

The class of health products most frequently suspected of causing the adverse reaction(s) was anticonvulsant agents (n=9), followed by anti-

infective agents (n=8), and antineoplastic agents (n=6). All three classes of health products are frequently used in paediatric care. The majority of the ADR reports described dermatological reactions.

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

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

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Bulimic eating disorders

March 2008 to February 2010

Highlights 2009

- In the second year of surveillance, 48 new cases of bulimic eating disorders were confirmed.
- Preliminary results seem to indicate that bulimic eating disorders are more commonly identified in adolescent years versus pre-adolescent years.
- Serious complications included bradycardia, hypokalemia and dehydration.

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 to 6%. Alarmingly, 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 comorbid 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 18th 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 12

BED cases in 2009

Reported	Duplicate	Excluded	Pending	Confirmed
84	1	0	35	48

In the second year of surveillance, 48 new cases of bulimic eating disorders were confirmed in children and adolescents aged five to 18 years. The mean age at presentation was 16 years (range 14–19 years). Eleven subjects (23%) were under the age of 16 years, and 37 (77%) were between 16 and 19 years. Four boys (8%) were identified. Preliminary results seem to indicate that bulimic eating disorders are more commonly identified in adolescent years versus pre-adolescent years.

Both bingeing and vomiting were found in 35 (73%) children and adolescents. The breakdown of symptoms can be found in Table 13.

TABLE 13

Eating disorder symptoms

Symptom	Frequency (n=48) (percentage)
Bingeing	43 (90%)
Vomiting	40 (83%)
Laxative abuse	11 (23%)
Diuretic abuse	1 (2%)
Other weight loss medication	11 (23%)
Exercise	37 (77%)
Food avoidance	40 (83%)
Fear of weight gain	46 (96%)
Preoccupation with food	45 (94%)
Preoccupation with body weight	46 (96%)
Perception that body is larger than it is	36 (75%)
Denial of severity of symptoms	21 (44%)
Somatic complaints	21 (44%)

Of the confirmed cases, 29 (60%) children and adolescents presented with at least one physical symptom. A breakdown of the physical symptoms can be found in Table 14.

TABLE 14

Other physical symptoms and signs

Symptom	Frequency (n=48) (percentage)
Bradycardia	6 (13%)
Tachycardia	3 (6%)
Hypokalemia	2 (4%)
Dehydration	8 (17%)
Dizziness	15 (31%)
Syncope	6 (13%)
Decreased gastric motility	9 (19%)
Gastro-oesophageal reflux	13 (27%)
Blood in vomit	6 (13%)

The mean duration of present illness was 18.6 months (\pm 13.3 months). In the previous six months, weight loss was reported in 33% (n=16) of cases, with a mean loss of 13 kg (range 2–30 kg) while weight gain was reported in 25% (n=12) of cases, with a mean gain of 7.6 kg (range 2–15 kg).

Less than half of the children and adolescents (n=16; 33%) did not have a current comorbid mental health diagnosis, while 33% had one comorbid diagnosis and 34% had two or more diagnoses. Twenty-five (52%) cases had a past history of a mental health disorder other than

bulimia or binge eating, and 36 (75%) had at least one family member with a history of a mental health disorder. Thirteen cases (27%) had a family history of an eating disorder and 25 (52%) of the subjects had a family history of depression.

Management included regular medical monitoring for 46 children and adolescents (96%), and in two cases this data point was left blank. Eight (17%) children and adolescents were hospitalized, and day hospital was the treatment listed for 11 cases (23%). The most common mental health intervention was individual therapy in 32 cases (67%) followed by family therapy in 27 cases (56%) and psycho-education in 25 cases (52%). Only 12 (25%) subjects received a psychotropic medication. Statistical analysis will be calculated upon completion of the surveillance. Study limitations include under-reporting due to the fact that some adolescents are seen by health care providers other than paediatricians.

Conclusion

Little data exists documenting the medical consequences or the treatment of bulimic eating disorder symptoms and behaviours in this population in the literature. This study provides one of the few venues to systematically report on the presence of medical findings in children and adolescents presenting with bingeing and/or purging.

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Congenital myotonic dystrophy

March 2005 to February 2010

Highlights 2009

- Nine of the 10 confirmed cases of CMD were index cases for their families.
- The phenotypes were more severe than seen in previous years, with one reported death.
- Prolonged hospitalizations were needed for respiratory dysfunction and feeding difficulties.

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.

In addition to the CPSP surveillance study, a separate parallel study was offered to reporting physicians to document outcomes.

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

TABLE 15

CMD cases in 2009

Reported	Duplicates	Excluded	Pending	Confirmed
30	14	3	3	10

In 2009, there were 30 cases reported. Of these, 10 met the inclusion criteria and were confirmed as incident cases, compared to eight and four in 2007 and 2008, respectively. Table 15 demonstrates that almost half the reported cases were duplicates and three are still pending. The cases were reported from five different provinces and territories. Of the 10 confirmed cases, four were male and five were

female, and in one case the gender is unknown. All but one of the cases were diagnosed before they reached one year of age; two were diagnosed with prenatal testing.

Because of respiratory dysfunction, seven children were ventilated for a period ranging from three to 191 days. Five of these received prolonged ventilation, lasting more than 30 days. Nine experienced feeding difficulties that led to prolonged hospitalization; eight required a nasogastric tube and one a gastrojejunal tube, for a period ranging from seven to 151 days. The number of CTG repeats is known for seven confirmed cases with a mean of 1,543 repeats (range 1,000–2,600). The most common complications were delayed gastric emptying, gastro-esophageal reflux and raised hemidiaphragm. There was one death; no additional information was provided on this child and the CTG repeat is unknown.

Nine children were the index cases for their families. In contrast to the majority of the index cases, where symptoms were evident at birth, one child was diagnosed in utero through amniocentesis that was performed because of polyhydramnios and decreased fetal movement. In the one case where the mother was aware of her myotonic dystrophy diagnosis, the baby was diagnosed with CMD during prenatal testing and went on to have symptoms at birth. In three 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.

Conclusion

With 10 confirmed cases in 2009, the study reached the expected number of 10–12 cases per year. The cases had more severe phenotypes than seen in previous years, with feeding difficulties being the main cause of prolonged admission to hospital in the newborn period. The incidence of prolonged ventilation was also higher this year. The CMD surveillance has confirmed 37 cases since the beginning of the study in 2005, which represents fewer cases than expected. 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.

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Publications and presentations

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Juvenile idiopathic arthritis

October 2007 to September 2009 – Final report

Highlights 2009

- Two years of JIA surveillance confirmed 846 incident cases.
- The median time from symptom onset to diagnosis was 4.3 months with the involvement of multiple health care providers.
- Although most children with JIA have a combination of joint pain, swelling and/or morning stiffness, some may have only joint pain or only joint swelling.
- To gain early disease control, the current standard of treatment includes non-steroidal anti-inflammatory medication, intra-articular steroid injections and a disease-modifying agent.

Background

Chronic arthritis in childhood, called juvenile idiopathic arthritis (JIA), is a rare condition of children and adolescents. The condition is long-term, and is one of the more common disorders resulting in chronic disability in children and adolescents. Children with JIA often suffer 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 16th birthday) who presented for the first time with:

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

Exclusion criteria

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

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

Results

TABLE 16

JIA cases from October 1, 2007 to September 30, 2009

	Reported	Duplicates	Excluded	Pending	Confirmed
2007*	149	2	1	0	146
2008	441	12	8	0	421
2009 †	297	0	10	8	279
Total	887	14	19	8	846

* October 1 to December 31, 2007

† January 1 to September 30, 2009

Demographic and epidemiologic data

A total of 887 cases of newly diagnosed JIA were reported during the two-year study period; of these, 846 were confirmed, resulting in an annual incidence of 4.3 new cases of JIA/100,000 children in Canada. Cases were reported through the CPSP and by paediatric rheumatology centres involved in an inception cohort research project on JIA called ReACCh Out (Research on Arthritis in Canadian Children, emphasizing Outcomes). Of the total confirmed cases, 328 were reported from ReACCh Out centres and, for the purpose of this report, only those reported through the CPSP (n=518) will be discussed. Future publications will present an analysis on all confirmed cases.

In accordance with previous literature, JIA was more commonly seen in girls (n=334, 65%) compared with boys (n=184, 35%).

The mean age at diagnosis was nine years (range 1–16 years). Of the cases reported through the CPSP, the majority were from Alberta (n=135, 26%), followed by Ontario (n=90, 17%), British Columbia (n=85, 16%), Manitoba (n=46, 9%), Nova Scotia (n=46, 9%), Quebec (n=42, 8%), New Brunswick (n=25, 5%), Saskatchewan (n=20, 4%), Newfoundland/Labrador (n=19, 4%) and Prince Edward Island (n=6, 1%). In four cases, the province or territory was not identified. No cases were reported by paediatricians in the territories; however, four cases were residents of the Northwest Territories, the Yukon or Nunavut.

Of the 518 confirmed cases, ethnicity data was available for 493 cases. The majority of these cases were Caucasian (82%). Other ethnicities included Asian (5%), First Nations or Inuit (4%), Black (1%), Middle Eastern (1%), and Latin American (<1%). In 5% of cases, the ethnicity was marked as 'other.' Of note, 52% of the Asian cases were reported from British Columbia. First Nations cases were reported from six provinces (British Columbia, Manitoba, Alberta, Saskatchewan, Quebec and Nova Scotia). Inuit cases were reported from Nunavut and Manitoba.

Prior to diagnosis, 20% of children were seen in an emergency room and 40% by a family doctor. Most children had consulted multiple health care providers prior to receiving a definite diagnosis of

JIA (mean 2, range 1–4). The median time from symptom onset to diagnosis was 4.3 months, with a range of 0–47 months.

Clinical features at presentation

The majority of patients were found to have joint pain, joint swelling and/or morning stiffness. A limp was less common, which is likely due to children who present with upper extremity arthritis only. Joint pain and swelling were reported in 83% of patients, with almost half (46%) reporting all four of the above symptoms. However, it is important to note that 17% of patients complained of joint pain without joint swelling and 9% were noted to have joint swelling without pain.

TABLE 17

Clinical features at presentation

Clinical features	Presence (n, percentage)	Absence (n, percentage)
Joint pain (n=509)	462 (91%)	47 (9%)
Joint swelling (n= 485)	403 (83%)	82 (17%)
Morning stiffness (n=462)	360 (78%)	102 (22%)
Limp (n=457)	323 (71%)	134 (29%)

The median number of affected joints at diagnosis was four (range 0–45). The most commonly affected joints were the knees, followed by the ankles and wrists.

JIA subtypes reported

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

For the 486 cases with complete subtype data, a subtype was assigned in 465 cases (Table 18). The most common JIA subtype was oligoarthritis. RF-negative polyarthritis was the second most common subtype, followed closely by enthesitis-related arthritis. Although relatively rare, significant numbers of children with RF-positive polyarthritis, psoriatic arthritis, and systemic arthritis were reported. The distribution of subtypes in this Canadian cohort is similar to that reported in the literature and other large JIA cohorts.

TABLE 18

Number of cases (n=486) and percentages of JIA subtypes

JIA subtype	Number of cases (percentage)
Oligoarthritis	217 (45%)
Polyarthritis RF-	85 (17%)
Enthesitis-related	83 (17%)
Polyarthritis RF+	30 (6%)
Psoriatic	28 (6%)
Systemic	22 (5%)
Unclassified	21 (4%)

Initial management of JIA

The majority of children newly diagnosed with JIA were given a non-steroidal anti-inflammatory medication, with the most common medication being naproxen (74%); however, 14% were not given a non-steroidal anti-inflammatory medication. Use of corticosteroid in the early treatment of JIA is not common, as only 25% of children received any corticosteroid, commonly as intra-articular injections. Of newly diagnosed children with JIA, 72 (14%) received an intra-articular corticosteroid injections, and these cases were all reported from paediatric rheumatologists. The majority of intra-articular injections were administered to children with oligoarticular JIA (54% of the injections). Methotrexate was prescribed as a disease-modifying agent for 20% of children at diagnosis, reflecting the current standard of early aggressive disease treatment of JIA.

Conclusion

During the two-year surveillance period, 846 cases of newly diagnosed JIA were confirmed through the CPSP and ReACCCh Out centres, resulting in an annual incidence of JIA of 4.3 per 100,000 children. Patients were reported from all provinces. The data are likely to be an underestimate of the true incidence of JIA, as some densely populated geographic areas of Canada were not fully reporting cases. Significant under-reporting and missed JIA diagnoses are also suspected in remote communities as some children might be treated by other health care professionals who are not participating in the CPSP. Of interest, only one previous report described cases of JIA from the Northwest Territories and Nunavut (Oen K, Schoeder M, Jacobson K, et al. *J Rheumatol* 1998). The cases

detected in this surveillance project were First Nations and Inuit in background and had been sent to paediatric rheumatology specialty centres for diagnosis. Other children and adolescents with JIA in these geographically isolated regions of Canada may not have received a diagnosis or early care for their arthritis due to poor access to medical care.

To date, the clinical presentations of the patients reported in this study are consistent with previously published studies, showing joint pain, swelling and stiffness as being the most frequent manifestations. It is important to note that a significant number of children with JIA may not have joint swelling or joint pain. Recognition of JIA in the early stages requires a high degree of suspicion in children or adolescents with persisting musculoskeletal complaints which do not resolve.

The most common JIA subtype is oligoarthritis, followed by RF-negative polyarticular and enthesitis-related arthritis. This latter type, a JIA subtype infrequently reported in epidemiologic studies, was documented in 17% of patients, making it relatively common. The three least common subtypes are psoriatic arthritis, RF-positive polyarthritis and systemic arthritis. Psoriatic arthritis, also sometimes not recognized as developing in childhood, was also reported as frequently as polyarticular RF-positive disease. Systemic onset JIA is a rare condition in childhood, with only 22 cases reported over the two-year time period.

The goals of treatment of children with JIA have changed over the past 10 years with paediatric rheumatologists aiming for complete disease control as quickly as possible. The early introduction of disease-modifying agents has become the standard of care and, more recently, children with JIA are being treated with new biologic agents. A significant percentage of children in the present study received an intra-articular corticosteroid injection or were started on a disease-modifying medication (methotrexate) from the time of diagnosis.

The study data demonstrates that JIA is seen across Canada and documents cases of JIA in Aboriginal children from the Northwest Territories, Yukon

and Nunavut. Further studies directed specifically at determining the true incidence of JIA among Aboriginal children need to be done to determine the burden of disease among this population. Most children with JIA are seen by multiple health care providers prior to diagnosis, suggesting insufficient awareness of this disease in childhood. Joint pain, swelling and morning stiffness are common presenting symptoms; however, clinicians must be aware that some children with only joint pain or only joint swelling do have JIA. Study results have shown that enthesitis-related arthritis, a subtype of JIA which is not generally recognized by many primary health care providers, is much more common than RF-positive polyarthritis and systemic onset disease. This study has also demonstrated the current standard of initial treatment for children with JIA in Canada, which now includes early intra-articular joint injections of corticosteroids, or disease-modifying agents for those with more severe subtypes of disease to optimize the care of children and youth with JIA.

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Publications and presentations

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

Kernicterus

January 2007 to December 2009 – Final report

Highlights 2009

- Kernicterus (chronic bilirubin encephalopathy) continues to occur in Canada, and rates appear to be decreasing post-publication of the 2007 Canadian Paediatric Society guidelines.
- ABO incompatibility, G6PD deficiency and sepsis are the most common causes of acute bilirubin encephalopathy leading to kernicterus.
- Almost all cases were diagnosed in infants less than one year of age, and long-term follow-up data will be required to confirm the extent of disabilities.

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 CPSP 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) Extrapyrimal 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 acidaemia type II, pyruvate dehydrogenase deficiency, Hallervorden-Spatz disease, neurofibromatosis type I, or children with carbon monoxide poisoning)

Results

TABLE 19

Kernicterus cases from January 1, 2007
to December 31, 2009

	Reported	Duplicates	Excluded	Pending	Confirmed
2007	17	3	1	1	12
2008	11	2	0	1	8
2009	6	0	1	3	2
Total	34	5	2	5	22

In the three-year study period, 22 cases of kernicterus (chronic bilirubin encephalopathy) were confirmed. Of the five pending cases, three occurred in 2009, and detailed questionnaires are expected. Interestingly, in all but two cases, 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=4), G6PD deficiency (n=3), sepsis (n=2), other antibodies (n=2), Rh isoimmunization (n=1), hemoglobinopathy (n=1) with pending G6PD results. In nine cases, the etiology was not available. Of the 22 confirmed cases, 12 (55%) had abnormal neurological findings. Hearing assessments were carried out by auditory brain stem testing in 17 cases (abnormal in 13). Confirmatory MRI scans of the brain were performed in 18 cases (abnormal in 15).

Using this very conservative estimate of 22 new cases of kernicterus over a three-year period (assuming a birth rate of 300,000/year), the estimated incidence of kernicterus would be 1:41,000 births.

The study data 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. In addition, the establishment of kernicterus as a diagnosis is often difficult and may be delayed. Both of these factors lead 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 (www.cps.ca/english/statements/FN/fn07-02.htm).

The intent of the new guidelines is to identify at-risk newborns in order 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.

The number of reported cases was lower in each subsequent year. The introduction of guidelines on the management of neonatal hyperbilirubinemia, including the recommending of universal measurement of infants' bilirubin in the first 72 hours of life, may be reducing the incidence of chronic bilirubin encephalopathy.

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.

Changes to the CPS guidelines have been made on the management of neonatal hyperbilirubinemia. Continued surveillance is necessary to assess the effectiveness of the guidelines and to determine whether additional strategies are needed to prevent kernicterus.

Given the young age of the infants reported, long-term follow-up data will be required to confirm the extent of their disabilities.

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Publications and presentations

Sgro M, Campbell DM, Shah V, Fallah S. The incidence of kernicterus in Canada 2007–2009. Canadian Paediatric Society Annual Conference, Ottawa, June 2009. (Poster presentation)

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

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Research Day, Mount Sinai Hospital, Toronto, April 2009. (Poster presentation)

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

Sgro M, Campbell D, Shah V. The incidence of kernicterus in Canada 2007–2009. Pediatric Academic Societies Annual Meeting, Honolulu, 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, May 2008. (Poster presentation)

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

Langerhans cell histiocytosis

July 2009 to June 2011

Highlights 2009

- In the first six months of surveillance, five cases of LCH were confirmed.
- The mean duration from first symptoms to diagnosis was 6.4 weeks with variable clinical presentations and the involvement of multiple health care providers.

Background

Langerhans cell histiocytosis (LCH) is a rare disease characterized by proliferation of pathogenic Langerhans cells causing infiltration and destruction of tissues. Presentations range from skin rashes and bony lumps to fulminant multisystem disease. Treatments range from observation, curettage or steroids, to chemotherapy and haemopoietic stem cell transplant for severe cases. Sequelae may be significant and patients may relapse. Reported incidence is 2.24 to 8.9 per million children from European data, but case ascertainment is difficult as diagnosis may be difficult or delayed, with patients referred to many different specialists. Little is known about pathways to diagnosis and management, etiology and ethnic susceptibility, especially in Canada. This study aims to: identify cases through the CPSP and parallel direct survey of associated specialists; generate Canadian epidemiological data; provide a platform for improving education about LCH; and establish a Canadian LCH Registry to aid patient management and research.

Objectives

Primary objective

The primary objective is to identify the epidemiological features of LCH in Canada.

Secondary objectives

- 1) Describe the patterns of presentation, clinical and pathological features of newly diagnosed LCH cases
- 2) Examine the pathways of referral and diagnosis of LCH cases
- 3) Identify the time delays from symptom onset to definitive diagnosis
- 4) Describe the initial treatment of LCH cases, including access to, and participation in, clinical trials

- 5) Compare Canadian data with other published epidemiological surveys to improve global knowledge of this condition

Case definition

Report any new patient presenting from birth to the 18th birthday with:

- Clinical LCH features that may include unexplained bone pain and soft tissue swelling, diabetes insipidus and hypothalamic-pituitary dysfunction, proptosis, recurrent otitis or otorrhoea, maculopapular rash or seborrhoeic dermatitis or napkin dermatitis resistant to treatment, interstitial pneumonitis or sclerosing cholangitis

AND

- Either a) or b)
 - a) Biopsy-proven LCH, with lesional cells containing:
 - Birbeck granules demonstrated on electron microscopy and/or
 - CD1a positive cells and/or
 - Langerin-positive cells and/or
 - S100 positive cells with characteristic H&E histopathology
 - b) Lytic bony lesions or pituitary/hypothalamic lesions characteristic of LCH without biopsy where:
 - Risks of biopsy are considered too hazardous due to site of lesion
 - Lesion has shown characteristic spontaneous regression

Results

TABLE 20

LCH cases from July 1 to December 31, 2009

Reported	Duplicates	Excluded	Pending	Confirmed
18	4	7	2	5

In the first six months of the study, five cases of LCH were confirmed. Seven cases were excluded either because the diagnosis was not LCH or because they were diagnosed before the start of the study. No additional cases have been reported through parallel direct survey of associated specialists. All five confirmed cases were male and of Caucasian background. The mean age at presentation was four years 11 months. Presenting symptoms included skull/scalp lumps (n=3), polyuria/polydipsia (n=1) and constipation (n=1). All cases had bony involvement: unifocal bone disease (n=3), multifocal bone and CNS “risk” disease (n=1), and multifocal bone and “risk organ” involvement (n=1), using staging criteria from the Histiocyte Society.

The confirmed cases are beginning to show the pathways of referral before final diagnosis and management. The mean duration from first symptoms to diagnosis was 6.4 weeks (range 2–13 weeks). Initially, patients presented to emergency room physicians (n=2), to paediatricians (n=2) and to a family physician (n=1). Subsequently, one was referred to paediatric endocrinology and two to paediatric neurosurgery prior to ultimate referral to paediatric haematology/oncology for definitive therapy. Of the three patients presenting with skull lumps, one had curettage alone, and two received adjunctive chemotherapy—one with steroid/vinblastine and one with steroid/vinblastine/6-mercaptopurine due to multisystem involvement.

One patient with bony vertebral disease received steroid/vinblastine as did the patient with diabetes insipidus. Currently, no clinical trials for LCH are open in Canada.

Conclusion

Although at an early stage, case reporting is continuing with steady case accrual. No clear conclusions can be drawn at this time. Interestingly, the mean duration from first symptoms to diagnosis is 6.4 weeks with multiple health care providers involved prior to diagnosis and definitive therapy. Integration of the parallel associated specialist survey is expected to provide external validation of the number of cases and quality of the data obtained. A similar study done by the British Paediatric Surveillance Unit will allow for international comparison.

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Methicillin-resistant *Staphylococcus aureus* in hospitalized children

September 2008 to August 2010

Highlights 2009

- The study confirmed 72 cases of hospitalized children with MRSA infections
- The mean length of hospital stay for children with community-acquired infection was 15 days.
- Of confirmed cases, 88% were community-acquired.

Background

Methicillin-resistant *Staphylococcus aureus* (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 76% of paediatric patients admitted to participating hospitals with MRSA had CA-MRSA. Limited information exists about the extent of the 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 21

MRSA cases in hospitalized children in 2009

Reported	Duplicates	Excluded	Pending	Confirmed
121	5	10	34	72

At the conclusion of the 2009 surveillance year, 72 cases of MRSA infections were confirmed with 34 cases pending (Table 21). Males comprised a slightly higher percentage (57%) of cases than females, and 73% of children were from urban areas. The mean age of confirmed cases is 5.1 years (range of six weeks to 17 years), with 28 (39%) being 12 months of age or younger. The geographical distribution of cases was as follows: Western Canada (51%), Central Canada (42%) and Eastern Canada (7%). The most significant presentations among confirmed cases, as summarized in Table 22, included 41 (34%) cases with skin or soft tissue infection, 13 (11%) with bacteremia, and 9 (8%) with pneumonia, while 55 (47%) had abscesses or other manifestations. Multiple manifestations were present in 23 children.

TABLE 22**MRSA: Clinical presentations upon admission in 2009**

Clinical site	N (%)
Skin / soft tissue	41 (34%)
Bacteremia	13 (11%)
Pneumonia	9 (8%)
Osteomyelitis	7 (6%)
Cervical adenitis/abscess	6 (5%)
Empyema	4 (3%)
Meningitis	4 (3%)
Septic arthritis	3 (3%)
Muscle infection	2 (2%)
Fasciitis	1 (1%)
Other	28 (24%)

Vancomycin was started in 16 (22%) patients as initial therapy. The mean length of hospital stay for children with community-acquired infection was 15 days (range 1–77 days). Sixty-three patients (88%) had community-acquired infection, whereas nine (12%) were thought to have acquired infection in a health care facility.

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, therefore, risk factors such as child care 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 2009 surveillance year. Study limitations include

under-reporting due to the fact that hospitalized children with MRSA are also treated by health care providers other than paediatricians, especially in community hospitals in rural or remote areas. Data on prevalence of known risk factors, associated infections and infection control precautions will be analyzed as the study continues. The final report will include all confirmed cases identified from September 2008 through August 2010 and a discussion on external validation of cases with the provinces and territories. These data are important and are needed to develop preventative strategies.

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Serious adverse events associated with paediatric complementary and alternative medicine

January 2009 to December 2010

Highlights 2009

- Few cases of suspected serious adverse events associated with paediatric complementary and alternative medicine have been reported.
- Harm may be “direct,” i.e., due to the therapy itself, or “indirect,” due to a delay in diagnosis or treatment.
- Clinicians are encouraged to ask about CAM use at every patient visit.

Background

Complementary and alternative medicine (CAM) is defined as a group of diverse medical and health care systems, practices and products that are not presently considered to be part of conventional medicine. In 2004, the largest Canadian paediatric study to date (n=1,804) found that 49% of the paediatric population seen in an urban paediatric emergency department reported CAM use, with half using natural health products (NHPs) and one-third using chiropractic.

Despite the frequent paediatric use of CAM, few studies thus far have assessed CAM-related adverse events (AEs) using a population-based approach. In 2006, the CPSP conducted a one-time survey on AEs associated with paediatric CAM. Seven percent of respondents had seen AEs following CAM use in the past year and 105 paediatricians reported 488 incidences of patients who had delayed diagnosis/treatment associated with CAM use. The survey did not distinguish between serious and non-serious events. These preliminary data set the stage for a two-year prospective study.

Objectives

- 1) Determine the number of CAM-associated AEs recognized by Canadian paediatricians
- 2) Generate detailed epidemiological descriptive data about serious AEs (both direct and indirect) associated with CAM use in children in Canada, including their nature and severity
- 3) Describe the clinical manifestations and risk factors of confirmed cases

Case definition

Any patient less than 18 years of age with a serious* direct or indirect† adverse event (AE) associated with the use of complementary and alternative medicine (CAM)§.

* Serious AE is defined as one that results in hospitalization, permanent disability, or death. Classification used by National Institutes of Health.

† Indirect AE refers to delays in diagnosis/treatment and/or inappropriate provision for a serious medical condition.

§ CAM is a broad umbrella term for a variety of practices and products that are not considered part of conventional medicine, such as chiropractic, massage therapy, and natural health products. Natural health products include vitamins and minerals, herbs, homeopathic medicines, traditional medicines, probiotics, and other products like amino acids and essential fatty acids.

Results

TABLE 23

Serious adverse events associated with paediatric CAM cases in 2009

Reported	Duplicate	Excluded	Pending	Confirmed
8	1	0	3*	4†

* Pending detailed questionnaires (n=2); pending adjudication (n=1)

† Confirmed suspected AEs; adjudication initiated; causality not yet determined

Table 23 presents cases reported for the first year of surveillance of a two-year study. At this interim stage, data results confirm that serious harm may be associated with paediatric CAM use as reported by CPSP participants. The reports of adverse events vary from anaphylaxis and hallucinations to muscle weakness with elevated creatine kinase. CAM therapies included bee pollen, HRP-C (also known as pigs' ears), pseudo-immunotherapy (a form of healing touch), and tea made from the datura plant. Indirect harm associated with CAM use was also

reported, such as a case of delay in treatment of juvenile idiopathic arthritis.

Importantly, this study has contributed to the development of an adjudicating algorithm to assess direct harm associated with CAM, whether product, practice, or device, as well as development of a new tool that is now being piloted to assess indirect harm. At present, the cases are reported as suspected AEs since they are being evaluated through an adjudicating algorithm to confirm causality and, therefore, cannot yet be reported as “confirmed.” At the study’s conclusion, the interpretation of data results will be both on the cases and the adjudicating algorithms that were developed to support case assessment.

Conclusion

Given the popularity of paediatric CAM use in Canada and around the world, their safety warrants formal evaluation.

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Severe combined immunodeficiency

April 2004 to March 2010

Highlights 2009

- In 2009, six cases of SCID were confirmed, two in Aboriginal children.
- Main clinical features include lymphopenia, interstitial pneumonia and failure to thrive.
- The average age of diagnosis was two months. Earlier diagnosis carries a better prognosis, as bone marrow transplantation can be performed before the appearance of overwhelming infections.

Background

Severe combined immunodeficiency (SCID) is a severe condition with high morbidity and mortality. As part of the strategy to reduce the incidence and severity of tuberculosis, the First Nations and Inuit Health Branch (FNIHB) of Health Canada has recommended the use of the BCG vaccine for newborns. Infants who have SCID and who receive the BCG vaccine are at high risk of severe complications from the vaccine. As part of a 2003 policy dialogue on the use of BCG, various stakeholders urged FNIHB to study the prevalence of SCID in Aboriginal populations in Canada to better inform decision making about the vaccine. Six cases of disseminated BCG infection in Aboriginal children were reported between 1993 and 2002, and four of them had SCID. The observed rate of disseminated BCG infection in Aboriginal 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.

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/mm³ or less than 20% CD3+ T cells;
- Familial history of primary immunodeficiency.

Exclusion criteria

Exclude infants with HIV infection or cystic fibrosis.

Results

TABLE 24

SCID cases in 2009

Reported	Duplicates	Excluded	Pending	Confirmed
13	5	0	2	6

Six cases of SCID were confirmed in 2009; two other cases are pending, awaiting further immunological data. Most of the cases were male, with only one female. All confirmed cases were born in Canada; one of them was a First Nations infant and one was an Inuit infant. Three cases reported a family history of immunodeficiency; none had received the BCG vaccine. The average age at diagnosis is two months (range 0–6 months). Two of the confirmed cases were of the ADA deficiency SCID-type, two were X-linked, and one was due to ZAP-70 mutation. The main clinical features documented were lymphopenia, interstitial pneumonia and failure to thrive. Examples of other infections included influenza H1N1, *Pneumocystis carinii* and osteomyelitis. At time of reporting, two cases had received a bone marrow transplant and three died before receiving it.

Discussion

Since April 2004, 35 SCID cases have been confirmed. Among these, there were four First Nations infants and one Inuit infant. The presence 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 2009, 2008 and 2007

were diagnosed at younger average ages than those reported in 2006 and 2005 (2 months, 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 (1 in 75,000–100,000 live births) and the annual birth rate in Canada, the expected number of new cases of SCID is three to five 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 during the period of the study are diagnosed and analyzed.

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Severe iron-deficiency anemia in infants and young children

October 2009 to September 2011

Highlights 2009

- Severe iron-deficiency anemia is being reported in infants and young children.
- The mean age at presentation was 15 months.
- Dietary factors were involved in confirmed cases.

Background

There is good evidence of major adverse health impacts associated with both severe and moderate iron-deficiency anemia (IDA) in otherwise healthy infants and young children. Severe, prolonged IDA may lead to congestive heart failure and ultimately death. Moderate anemia may be associated with changes in motor and cognitive development in young children.

The Canadian Paediatric Society (CPS) recommends exclusive breast-feeding for six months, followed by the introduction of iron-containing complementary foods. These two recommendations should prevent anemia from developing in most full-term infants. Although cow's milk is an important food for the growing child, the CPS recommends restricting its introduction until after nine months of age, while the American Academy of Pediatrics (AAP) recommends restricting its introduction until after 12 months of age. Factors associated with the development of severe IDA in older infants are less well understood.

Objectives

- 1) Ascertain the incidence of severe IDA among otherwise healthy Canadian infants and young children by identifying all newly diagnosed cases over a two-year period
- 2) Determine the significant health complications of severe IDA, such as urgent paediatric consultation, emergency department care or hospitalization, need for blood transfusion or the development of congestive heart failure
- 3) Determine the ethnicity of infants and young children presenting with severe IDA

- 4) Obtain demographic and medical information which will assist in:
 - the identification of risk factors for development of severe IDA in Canada
 - the evaluation of current preventive strategies
- 5) Supply data that will help develop novel public health policies to prevent severe IDA among children living in Canada
- 6) Determine adherence to the CPS recommendation on exclusive breastfeeding for six months and restriction of cow's milk until after nine months of age in children with severe IDA in Canada

Case definition

Report all otherwise healthy infants and young children from six months to 36 months of age with severe iron-deficiency anemia defined as:

Hemoglobin <80 g/L and low mean corpuscular volume (MCV; below normal for age) **plus one or more of the following:**

- low ferritin
- low iron
- high transferrin receptor
- high free-erythrocyte protoporphyrin
- correction of anemia with iron therapy

Exclusion criteria

- Chronic disease known to be associated with anemia
- Diseases associated with malabsorption
- Conditions associated with blood loss, such as trauma, surgery, and frequent bloodletting
- Known congenital hemoglobinopathy
- Known disorders of clotting
- Blood loss due to acute or chronic disease causing gastrointestinal bleeding

Results

TABLE 25

Severe IDA cases from October 1 to December 31, 2009

Reported	Duplicate	Excluded	Pending	Confirmed
33	0	10	14	9

In the first three months of surveillance, 33 cases of severe iron-deficiency anemia have been reported in infants and young children. Ten cases have been excluded for the following reasons: diagnosed before the start of the study (n=8) and missing a confirmatory biochemical laboratory test such as ferritin (n=2). The remaining 14 cases are either pending or under review and nine cases have been confirmed to meet the case definition. Mean age was 15 months (range 6–27 months). Ethnicity was Caucasian (n=3), Aboriginal (n=2), Asian (n=2), South Asian (n=1), African (n=1). The mean hemoglobin level was 56 g/L (range 34–81 g/L), mean MCV was 50.7 fL (range 46–62.5 fL), mean serum ferritin 3.4 µg/L (excluding one patient with a ferritin of 52 µg/L in the context of an acute infectious illness and good response to oral iron therapy). Six infants were currently or previously breast-fed. Of the five infants currently receiving cow's milk, the mean daily consumption was 984 mL (32.8 oz), range 480 mL to 1.8 L (16–60 oz), and five of nine were reported to have inadequate meat intake. Presenting signs included pallor (n=5), seizure (n=1), developmental delay (n=2) and preoperative screening (n=1). One infant had a cerebral sinus venous thrombosis, and three

had evidence of developmental delay. In all cases, the attending physician prescribed oral iron supplementation and provided dietary counseling. Three were admitted to hospital and one child required a blood transfusion.

Conclusion

The early results from the first three months of surveillance demonstrate that severe IDA is being reported in Canadian infants and young children. Results are too preliminary to identify the most important risk factors; however, dietary factors were involved in confirmed cases.

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Travel-related illnesses in paediatric travellers who visit friends and relatives abroad

March 2009 to February 2011

Highlights 2009

- In the first 10 months of surveillance, 30 confirmed cases of significant travel-related illnesses occurred among paediatric travellers who visited friends and relatives abroad.
- Enteric fever (“typhoid fever”), malaria and hepatitis A were the most common types of travel-related illnesses.
- A minority of cases were confirmed to have obtained pre-travel advice.
- Almost two-thirds required hospitalization with an average length of stay of seven days; one death was reported.

Background

Over 7.4 million Canadians travelled internationally in 2007. An estimated 4% of these are children; consequently, almost 300,000 Canadian children travel internationally each year. People who visit friends and relatives abroad (VFRs) account for approximately 40% of international travellers; therefore, up to 100,000 Canadian children may travel as VFRs each year.

Travel-related illnesses in paediatric travellers (TRIP) are an important public health issue, since these children account for a disproportionate number of travel-related hospitalizations. In particular, VFRs are known to be at significantly increased risk of travel-related illnesses (TRIs), including enteric fever, hepatitis A and malaria, which are potentially preventable by pre-travel interventions such as vaccinations, anti-malarial medications and insect precautions. Paediatric VFRs represent a significant number of international travellers from Canada who are at greater risk of travel-related illnesses; however, little data is available regarding the incidence and epidemiology of these illnesses among paediatric VFRs.

Objectives

- 1) Determine the number of significant travel-related illnesses among paediatric VFR travellers living in Canada
- 2) Determine the epidemiology of significant travel-related illnesses among paediatric VFR

travellers, including the countries of travel, duration and type of travel, time of year travel occurred, timing and types of illnesses

- 3) Describe clinical manifestations and severity of illnesses at presentation among paediatric VFR travellers
- 4) Identify risk factors for significant travel-related illnesses among paediatric VFR travellers (e.g., pre-travel health advice and compliance, countries of travel, ingestion of high-risk food and water, malaria prevention measures used)

Case definition

A travel-related illness is acquired while travelling abroad and symptoms may develop during travel or following the child's return to Canada. A VFR traveller may be a foreign-born child or the Canadian-born child of foreign-born parents who is travelling to a country of origin to visit friends and relatives. The diagnosis is made on clinical and/or laboratory criteria.

Report all children living in Canada less than 18 years of age who acquire significant travel-related illnesses while travelling abroad as VFR travellers.

Exclusion criteria

- Children who develop travel-related illnesses but did not travel to visit friends and relatives
- Children who acquire non-specific mild travellers' diarrhea and respiratory infections, not requiring hospitalization

Results

TABLE 26

TRIP-VFR cases from March 1 to December 31, 2009

Reported	Duplicate	Excluded	Pending	Confirmed
50	1	8	11	30

In the first 10 months of surveillance, the study confirmed 30 cases of travel-related illnesses in paediatric VFRs. Among these, 16 (53%) were reported from Ontario, eight (27%) from British Columbia and Alberta, and six (20%) from Manitoba and Quebec. The regions of travel and the types of TRIs acquired by paediatric VFRs are summarized in Figure 4 and Table 27.

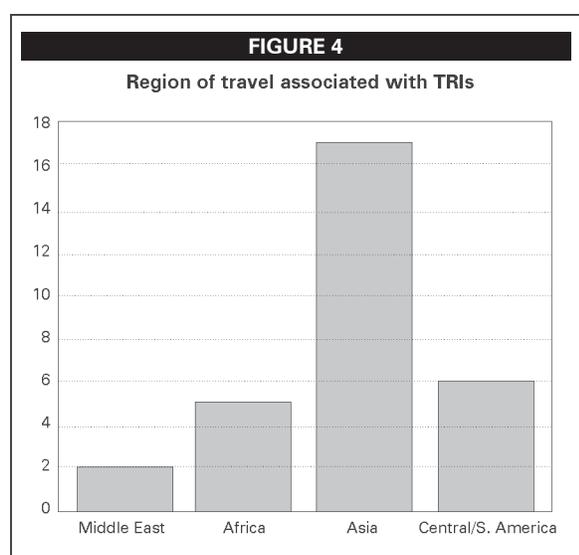


TABLE 27

Types of TRIs acquired by paediatric VFRs

Enteric fever (suspected/confirmed)	11 (3/8)
Hepatitis A	4
Malaria	4
Parasitic infections	3
Severe diarrheal illness	3
Severe respiratory illness	2
Dengue	1
Sepsis	1
TB symptomatic disease	1

The majority (70%) presented with fever. Diarrhea (40%), vomiting (20%), abdominal pain (20%), and headache (17%) were also common symptoms. Three-quarters (75%) of the malaria

cases presented with gastrointestinal or respiratory symptoms as well as fever. More patients with TRIs were initially seen in the emergency department (60%) than in the office or clinic (40%).

The interval of time between the beginning of travel and the onset of symptoms ranged from a few days to several weeks. The interval of time between the onset of symptoms and the physician visit varied depending on the type of travel illness, as did the time between the onset of symptoms and diagnosis.

The average duration of travel was approximately five weeks. Almost half of the VFR children travelled exclusively to urban areas; 15% to rural locations only and 37% to both rural and urban areas. All confirmed cases, whose type of accommodation was known, stayed in family homes, only 10% of which were documented to have air-conditioning and/or insect screens. Other risk factors included ingestion of food from street vendors (17%), unsafe water (30%), unpasteurized dairy products (7%), and uncooked or unpeeled fruits and vegetables (27%).

Among the 30 confirmed cases, 12 obtained pre-travel advice, 10 did not, and in eight cases it was unknown whether they received any. Of those who received pre-travel advice (n=12), six obtained it from a travel clinic, three from a paediatrician, two from a family doctor, and one respondent did not specify by whom the advice was provided. Of those who went to a travel clinic, two met with a nurse, two with a physician, and two did not specify the type of health care professional they saw.

Of those who obtained pre-travel advice, the reporting physician questioned the appropriateness of advice in two cases: one patient received only a hepatitis A vaccine when a typhoid vaccine should also have been given, and a family was told that children did not need anti-malarial prophylaxis although the parents were given prophylaxis. In three cases, the advice was not followed, and in six cases it was unknown if the advice was given correctly and not followed or was inappropriate. A primary vaccine failure was reported in one case with enteric fever, despite the administration of a typhoid vaccine. Of note, the effectiveness of typhoid vaccines is known to be only about 70%.

Adequate food and water precautions, in addition to the vaccine, should have decreased the risk.

Almost two-thirds of patients with TRIs required hospitalization (n=19) with an average length of stay of seven days. There was one death due to septic shock.

Conclusion

In the first 10 months of surveillance for significant travel-related illnesses among paediatric VFRs, there were 30 confirmed cases. This number likely under-represents the burden of TRIs among paediatric VFRs, because the case definition excludes mild respiratory and gastrointestinal illnesses that do not require hospitalization.

The results of this surveillance are consistent with information regarding TRIs among adults, given that the paediatric VFRs generally travelled for several weeks, stayed in family homes, and ingested unsafe food and water. The majority of TRIs occurred in children who travelled to Asia. Less than half of the paediatric VFRs sought travel advice, and among those who did, 50% obtained advice from a travel medical clinic.

The majority of paediatric VFRs required hospitalization for their TRIs with an average length of stay of seven days. In addition, there was one death. Consequently, there is significant

morbidity and mortality among paediatric VFRs in Canada. Furthermore, almost all of the TRIs were potentially preventable if appropriate pre-travel advice had been obtained and followed. This highlights the need for increased education of families and health care providers regarding the importance of pre-travel advice to minimize the risk of acquiring travel-related illnesses, particularly for paediatric VFRs.

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Publications and presentations

Crockett M, Hui C, Kuhn S, Ford-Jones L, Keystone J. Travel-related illnesses in Canadian children (TRIP study). Infectious Diseases Society of America Annual Meeting, Philadelphia, October 2009. (Poster presentation)

Survey Questions

Congenital cytomegalovirus infection – Post-study survey

February 2009

From March 1, 2005 to February 28, 2008, the CPSP conducted surveillance for congenital cytomegalovirus (cCMV) infection. One of the educational goals of this surveillance was to increase Canadian paediatricians' awareness of the most effective way to make a cCMV diagnosis. Cytomegalovirus (CMV) serology in the newborn is a poor way of identifying congenital infection. Although the presence of IgM is very specific for fetal and newborn infection because IgM does not cross the placenta from the maternal circulation and, hence, indicates fetal infection, it is not very sensitive. Congenital CMV infection usually begins early in gestation, particularly when it results in significant symptomatic sequelae. The fetus does not mount a significant immune response and, in fact, develops immune tolerance for the virus. Isolation of the virus or detecting viral DNA by polymerase chain reaction (PCR) is a very sensitive and specific method of making the diagnosis. Because of the overwhelming fetal infection with minimal immune response, there are massive quantities of virus being excreted in the urine and saliva. Viral isolation must occur during the first three weeks of life, as isolation beyond that age may indicate acquired infection (from breast milk or other community sources) and is not definitive for the diagnosis of congenital infection.

Before launching the study, participants were surveyed to assess their knowledge about the most effective way to confirm the diagnosis. Pre-study results were collated and reported as part of an educational highlights article at the start of the surveillance in March 2005.¹ As the case definition demands diagnosis within the first three weeks of life with either viral isolation or positive IgM,

participants received a copy of the case definition, study protocol, monthly surveys and a detailed questionnaire for reporting a case. These served as potential sources of education. Highlights and reports presented in *Paediatrics & Child Health*, the CPS journal^{1,2} and at the 2008 CPS Annual Conference^{3,4} were also educational opportunities.

Did any of this make a difference? One of the CPSP goals is to “raise awareness”⁵ amongst participants, and the program is looking at different ways of achieving this goal. The program therefore sought to determine if there was a change in the knowledge level of the participants with respect to the most effective way to make the diagnosis. A post-study survey was sent asking the same question as in the pre-study survey. The response rate for the pre-study survey (2005) was 32% and for the post-study survey (2009) only 17%. Results are presented in Table 28.

TABLE 28

Summary of cCMV survey results

“You see a three-day-old infant in the newborn nursery who has symptoms and signs suggestive of congenital CMV infection. If you had to choose only one test to confirm this diagnosis, which one of the following tests would you order?”

	2009 post-study	2005 pre-study
Answer	Number (percentage)	Number (percentage)
1. CMV IgG and IgM on cord blood	36 (9%)	117 (15%)
2. Throat swab for CMV culture or PCR	5 (1%)	10 (1%)
3. Torch serology	18 (4%)	82 (10%)
4. Urine specimen for CMV culture or PCR	348 (83%)	537 (68%)
5. Unknown	13 (3%)	34 (4%)
Incomplete	1 (0%)	6 (2%)
Total	421 (100%)	786 (100%)

The responses differed before and after the study: the percentage of paediatricians correctly choosing urine specimen for CMV testing increased from 68% to 83%; the percentage who selected incorrect serology answers (1 and 3) decreased from 25% to 13%; and the percentage who correctly chose viral isolation answers (2 and 4) increased from 70% to 84%.

The proportion of paediatricians who answered the survey question correctly was higher after the completion of the study. A limitation of the data is that survey responses were anonymous and unlinked; it is unknown who repeated the survey and whether the same respondents who responded correctly the first time were more likely to respond this time. While more respondents answered correctly, it is unknown whether non-respondents were less likely to respond correctly. Samples have been treated as independent in the analysis.

Despite the low response rate of the post-study survey, the change in knowledge level suggests the ability of the program to raise awareness of a condition and educate CPSP participants, while generating valuable epidemiological data about rare high-impact conditions in Canadian children. The program will need to explore various ways of documenting increased awareness amongst participants.

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Web-based reporting

July 2009

The CPSP is seeking a viable solution for electronic relay of data and information resources among participants, staff and investigators. This process reflects the program's desire to administer the CPSP

responsibly. The objectives for implementing such a system are to enable faster communications; facilitate reporting by providing immediate access to study case definitions and protocols; and reduce materials, postage costs and production times. The system must maintain or improve response rates and enable rapid-response data capture, especially in face of an emerging health concern.

To better understand the need for an electronic reporting system, the CPSP used a variety of research tools, including a mailed survey to participants, in-depth interviews and focus groups.

The overall survey response rate was 31% (756 respondents). Responses were received from most provinces and territories. More than two-thirds of participants indicated a willingness to report on-line, 13% were undecided and would require further information, and 15% preferred status quo. For this last category, a parallel hard-copy system will remain in place.

Of the respondents who were unsure about on-line reporting, issues such as aptitude and access to technology, additional e-mail burden, and the tendency to miss e-mails, were among the top reasons that explained the hesitancy to adopt such a system.

Suggestions for successful implementation included a simple, quick and reliable system with minimal or no log-in requirements, e-mail reminders to report with links to Web forms, and the highest levels of security.

Participants were also asked about the use of CPSP resources on-line, specifically ADR Tips of the Month, quarterly updates, educational resources and study protocols. Even if some participants were willing to report on-line, they indicated a preference for continuing to receive hard copy resources.

The program is currently in consultation with potential suppliers and will provide feedback on the progress of implementing an electronic system. Participants will be contacted regularly to ensure a user-friendly system. Future steps will include investigating the option of completing detailed questionnaires on-line and possibly enhanced features such as real-time statistics.

The CPSP would like to thank all the participants and investigators who generously gave their time to provide input and suggestions for implementing Web-based reporting.

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Paediatric antiviral drug use and potential adverse reactions

December 2009

In June 2009, the World Health Organization declared a worldwide pandemic in regard to a novel strain of influenza virus, the influenza A (H1N1) virus. This novel infection was considered a serious and life-threatening disease and had been associated with several fatalities. In July 2009, the federal Minister of Health issued an Interim Order, permitting the expanded use of the antiviral drug, oseltamivir, for the treatment of influenza A (H1N1) infection in children less than one year of age. That decision was based on the results of pre-clinical toxicology studies in animals and the paucity of data available in children. The Interim Order called for enhanced pharmacovigilance activities in order to detect safety signals early. Surveying front-line health care providers was a component of such enhanced pharmacovigilance.

The CPSP, in collaboration with the Marketed Health Products Directorate (Health Canada), conducted a survey to assess the occurrence of serious and life-threatening adverse reactions (ARs) with the paediatric use of two antiviral drugs, oseltamivir (Tamiflu®) and zanamivir (Relenza®). Although the Interim Order applied only to oseltamivir, Health Canada and the CPSP decided to include both antiviral drugs in the survey, as both are used for prophylaxis and/or treatment of influenza infection in children.

The survey was sent to all 2,532 CPSP participants in the first week of December 2009. Paediatricians were asked to respond to questions regarding antiviral drug prescriptions and suspected ARs for the previous one-month period. Responses received

by Health Canada up to January 29, 2010, were reviewed. The response rate was 27%.

Prescriptions for at least one antiviral drug were reported by 74% (524/707) of the paediatricians who responded to the CPSP survey. When the drug prescribed was mentioned, the majority of prescriptions were for oseltamivir: 498 vs. 20 prescriptions for zanamivir. Oseltamivir was prescribed to children less than one year of age by 53% of physicians who reported prescribing antiviral drugs.

There were 21 reports of serious ARs associated with the use of oseltamivir. They were associated with the following systems:

- Gastrointestinal: Nausea, vomiting and diarrhea, hepatitis and pancreatitis
- Neuropsychiatric: Confusion, delirium, psychosis
- Renal: Acute renal failure
- Hematologic: Idiopathic thrombocytopenic purpura
- Dermatologic: Diffuse abrupt onset rash with conjunctival injection.

There were two reports of serious ARs associated with the use of zanamivir. One report listed “query pancreatitis;” the other report did not mention the specific reaction.

In conclusion, more than half of respondents confirmed they prescribed oseltamivir to children less than one year of age, and the survey documented 21 reports of associated serious ARs. Causality assessment (i.e., evaluation of the likelihood that the reaction is causally linked to the drug) was not the primary objective of the survey, and the data submitted did not allow for such assessment. Therefore, no causal inference can be made.

This one-time survey question enabled the CPSP to work in close collaboration with Health Canada and the Public Health Agency of Canada on an enhanced surveillance monitoring project to generate real-time preliminary data related to emerging health concerns in children.

Principal investigator

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International Developments



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

Currently, there are 13 national paediatric surveillance units worldwide that are full members of INoPSU: Australia, Britain, Canada, Cyprus/Greece, Germany, Ireland, Latvia, Malaysia, Netherlands, New Zealand, Portugal, Switzerland, and Wales. The British Ophthalmological Surveillance Unit is an associate member.

2009 highlights

The 2009 H1N1 pandemic influenza provided INoPSU with an excellent opportunity to work with national public health departments, to support research into the emerging epidemiology of this virus, to document complications such as Guillain-Barré syndrome in children, and to identify adverse reactions possibly related to the use of antiviral medication or the administration of the vaccine.

In 2009, a peer-reviewed highlights article on the “Public health impacts of the International Network of Paediatric Surveillance Units” was published to summarize international study results that have impacted public health and clinical care practices over the years. The article also provided

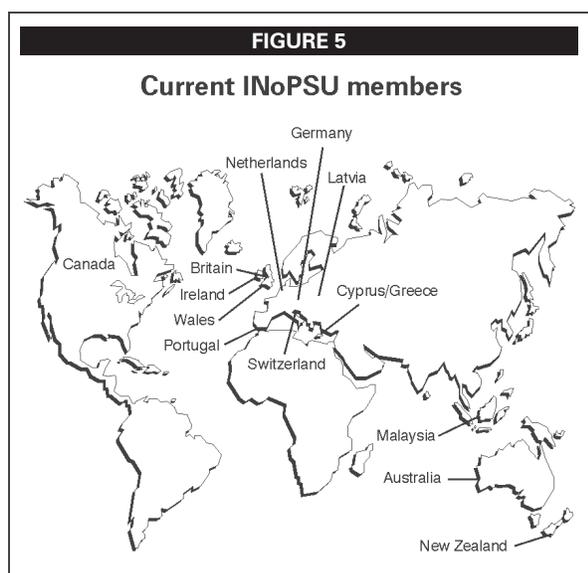


TABLE 29

National studies contributing to public health actions*

	APSU	BPSU	CGPSU	CPSP	ESPED	NSCK	NZPSU	SPSU	WPSU
Congenital cytomegalovirus infection	x	x		x					
Early-onset eating disorders	x	x		x		x			
Haemolytic uraemic syndrome	x	x		x	x	x	x	x	
Neonatal herpes simplex virus infection	x	x		x	x		x	x	
Pertussis	x		x		x	x	x	x	
Seat-belt syndrome	x			x					
Vitamin D deficiency rickets	x			x					x
Vitamin K deficiency bleeding	x	x		x	x	x	x	x	

* See legend of INoPSU members on page 51.

Table adapted from: Public health impacts of the International Network of Paediatric Surveillance Units. *Paediatr Child Health* 2009;14(8):499-500

timely data that informed the development of new policies and legislations. Table 29 provides an overview of the type of studies conducted by several units, which have provided the basis for international comparison.

INoPSU is currently developing a study database to link investigators for protocol sharing and data comparison. So far, INoPSU has facilitated the surveillance of over 200 conditions, of which 49 have been studied in more than one country. Further information on all national paediatric surveillance units can be obtained from the INoPSU Web site at www.inopsu.com. For the latest e-newsletter, visit www.inopsu.com/publications/E-newsletter.html.

Highlights from international meetings

In 2009, the CPSP participated in the 20th European Society of Paediatric and Neonatal Intensive Care (ESPNIC) Medical and Nursing Annual Congress and in the 50th European Society of Paediatric Research (ESPR) Annual Meeting with the following respective poster presentations: “The international paediatric surveillance network: Research in action” and “Active neonatal disease research through surveillance: The Canadian experience.” Both posters stimulated interest and discussion.

Interestingly, the Australian Paediatric Surveillance Unit convened a rare diseases working group, consisting of researchers, clinicians and representatives from parent support groups. The unit called for a national response to the significant impacts of rare childhood diseases in Australia and is planning a first rare diseases workshop in 2010. Other INoPSU members are engaged in similar initiatives within their respective countries.

Preparations are well underway for the sixth INoPSU conference, which will be held in Dublin, Ireland, October 7–8, 2010. The meeting will be hosted by the Faculty of Paediatrics of the Royal College of Physicians of Ireland.

TABLE 30

**Studies under surveillance
by national paediatric surveillance units in 2009**

Study	National Paediatric Study Surveillance Units
Acute encephalitis/encephalomyelitis	PPSU
Acute flaccid paralysis	APSU, BPSU, CPSP, NZPSU, SPSU
Acute post streptococcal glomerulonephritis	NZPSU
Acute rheumatic fever	APSU, SPSU
Adolescent pregnancy	LPSU
Adrenal insufficiency	IPSU
Adverse drug reactions – serious and life threatening	CPSP, NZPSU
Alcohol intoxication	NSCK
Anaphylaxis (immunization)	BPSU, ESPED, SPSU
Asthma difficult to treat	NSCK
Bulimic eating disorders	CPSP
Cerebral palsy among five-year-olds	PPSU
Children without legal status	NSCK
Chronic fatigue syndrome	NSCK
CNS inflammatory demyelinating disease	BPSU
Complementary and alternative medicine – serious adverse events	CPSP
Congenital adrenal hyperplasia	BPSU
Congenital cytomegalovirus infection	APSU, PPSU
Congenital myotonic dystrophy	CPSP
Congenital renal or urological defects	NSCK
Congenital rubella syndrome	APSU, BPSU, NZPSU, SPSU
Congenital toxoplasmosis	CGPSU, PPSU, SPSU
Conversion disorder	BPSU
Craniosynostosis	WPSU
Cystic fibrosis	NSCK
Diabetes mellitus	LPSU, PPSU, ESPED
EBV-associated lymphoproliferative diseases in non-immunocompromised children	ESPED
Epilepsy (deaths)	WPSU
Epistaxis in infancy	WPSU
Extended-spectrum β -lactamase-producing enteric Gram-negative bacilli	SPSU
Fetal alcohol syndrome	NSCK
Gallstones	WPSU
Group B streptococcal sepsis	PPSU
Group B streptococcal / <i>Escherichia coli</i> infections (invasive neonatal)	ESPED
Hemoglobinopathy	NSCK
Hemolytic uremic syndrome	CGPSU, PPSU, SPSU
HIV/AIDS (perinatal HIV exposure)	APSU, BPSU, NZPSU

Hyperbilirubinemia	NSCK, SPSU
Hypernatremia – severe	BPSU
Idiopathic intracranial hypertension (pseudotumor cerebri)	BPSU
Inborn errors of metabolism	NZPSU
Influenza, Influenza A/H1N1	APSU, ESPED
Interrupted pregnancy in adolescents	LPSU
Intussusception	APSU, BPSU
Iron-deficiency anemia – severe	CPSP
Juvenile dermatomyositis	ESPED
Juvenile idiopathic arthritis	CPSP
Kawasaki disease	NSCK, PPSU
Kernicterus	CPSP
Langerhans cell histiocytosis	CPSP
Leukemia, Transient leukemia in Down syndrome	LPSU, NSCK
Life-threatening event and unexplained death in neonates on the first day of life	ESPED
Long-term ventilation	WPSU
Lymphoma: Hodgkin's, non-Hodgkin's	LPSU
Measles (complications)	ESPED
Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA)	CPSP
Multiple sclerosis/ADEM	NSCK, ESPED
Neonatal bacterial or fungal infection in the first week of life (proven)	NZPSU
Neonatal herpes simplex virus infection	APSU
Neonatal hypoxic-ischaemic encephalopathy	WPSU
Neurological defects because of rotavirus infections	ESPED
Neuromuscular disorders	APSU
Osteitis, non-bacterial/bacterial osteomyelitis	ESPED
Pertussis	SPSU
Pneumococcal sepsis/meningitis	ESPED
Progressive intellectual and neurological deterioration (PIND)	BPSU
Rett syndrome	APSU
Severe combined immunodeficiency	CPSP
Shaken baby syndrome	ESPED
Sinus venous thrombosis, neonatal	ESPED
Sudden unexpected early postnatal collapse	BPSU
Systemic lupus erythematosus	APSU
Toxic shock syndrome	BPSU
Travel-related illnesses in paediatric travellers who visit friends and relatives abroad	CPSP
Varicella (neonatal, congenital, and complications)	APSU, IPSU, PPSU
Vitamin K deficiency bleeding/HDNB	APSU, 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
MPSU	Malaysian 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

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

Average track record

- 80% response from approximately 2,500 paediatricians
- 91% data completion rate

Study ideas

To encourage international collaboration, the CPSP invites researchers to submit proposals for studies currently or previously conducted by other national paediatric surveillance units, such as:

Bronchiectasis (APSU, NZPSU)

Celiac disease (IPSU, NSCK, WPSU)

Congenital adrenal hyperplasia (APSU, BPSU, NSCK, WPSU)

Congenital syphilis (BPSU)

Chylothorax (BPSU)

Fatal and near-fatal asthma (ESPED, MPSU)

Gonorrhoea, syphilis, chlamydia and trichomonas infections (BPSU)

HIV infections (APSU, BPSU, NZPSU, MPSU, NSCK)

Hypernatremia (BPSU, WPSU)

Idiopathic intracranial hypertension (BPSU)

Imported malaria (BPSU)

Life-threatening events / unexplained deaths (first day of life) (BPSU)

Moderate and severe encephalopathy (NZPSU, WPSU)

Rett syndrome (APSU, BPSU)

Systemic lupus erythematosus (APSU)

Tuberculosis (WPSU); tuberculous meningitis (IPSU)

Varicella/zoster, shingles (IPSU, PPSU, SPSU)

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



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

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



**For more information on the
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Canadian Paediatric Society

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