



CPSP

CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM



2010 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.



www.inopsu.com

Extending surveillance beyond borders

In 2010, the CPSP and the Australian Paediatric Surveillance Unit became co-chairs of the International Network of Paediatric Surveillance Units (INoPSU) that joins 12 diverse countries.

Mission

To advance the knowledge of rare, high-impact childhood conditions through the participation of paediatricians in surveillance on a national and international basis.

Scope

- INoPSU members conduct surveillance in a population of over 46 million children
- Globally, more than 8,000 clinicians contribute to the network
- Nearly 200 different rare conditions have been surveyed to date.

Communications (Administrative centre in the UK)

- Connects researchers in different countries
- Allows for sharing of study protocols
- Supports newly starting units
- Coordinates bi-annual conference
- Shares information via e-mail, newsletters and INoPSU website.

Strengths

- Excellent forum to discuss rare disease surveillance methodology
- Great opportunity to compare national results to those of other INoPSU members

- Fast and coordinated response to emerging public health concerns
- Ability to build on each other's experiences.

Future goals

- Expand the network to other countries
- Encourage publication of collaborative/comparative papers
- Participate in International Rare Disease Day
- Present study results at national and international conferences
- Establish closer contacts with other organizations such as EURORDIS¹, Orphanet², and NORD³
- Prepare for INoPSU's 15th anniversary conference in 2013.



1. EURORDIS: Rare Diseases Europe • 2. Orphanet: Reference portal for information on rare diseases and orphan drugs • 3. NORD: National Organization for Rare Disorders (US)

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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 the acute flaccid paralysis study 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 2010 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
- Manitoba Institute of Child Health
- Manitoba Medical Service Foundation
- Myasthenia Gravis Ontario Chapter, Muscular Dystrophy Canada
- Psychiatry Endowment Fund, The Hospital for Sick Children
- St. Michael's Hospital Innovation Fund
- Tara and Bobby Disenhouse Fund
- The Hospital for Sick Children Foundation
- William Singeris National Centre for Myotonic Dystrophy Research

Foreword

Chief Public Health Officer of Canada

As Chief Public Health Officer of Canada, I am very proud to accept the 15th Annual Report of the Canadian Paediatric Surveillance Program (CPSP).

Year after year, this program provides important information that promotes the health of Canada's children and youth.

CPSP has also proven itself an invaluable resource, providing rapid responses from member paediatricians to requests for data on emerging public health issues. Information gathered through the program also informs policy discussions and helps us gauge the potential impact of new policies and programs.

Canada's medical community, our health policy makers and members of the Canadian public continue to share the benefits of CPSP's insights and the surveillance work performed so effectively.

I would like to extend my thanks to the CPSP Steering Committee, Canadian Paediatric Society staff and Public Health Agency of Canada staff for their continued support of the surveillance program.



Dr. David
Butler-Jones

Federal Minister of Health

The 15th anniversary of the Canadian Paediatric Surveillance Program is one that deserves special recognition.

The CPSP has grown substantially since it was launched. It now gathers information from more than 2,500 paediatricians and other specialists about rare diseases and conditions in Canadian children. That information helps us learn more about these diseases and what we can do to prevent them. The CPSP data will help guide future health policies in Canada and around the world.

The CPSP could not succeed without the contributions of Canada's paediatricians and other specialists. Your dedication is helping improve the health of our children.

I would also like to thank the Canadian Paediatric Society (CPS) for its leadership in this important program.

The Government of Canada is proud to work with the CPS and its members, along with the provinces, territories and other partners, to provide a healthier future for Canadian children.



The Honourable
Leona Aglukkaq

President of the Canadian Paediatric Society

As President of the Canadian Paediatric Society, I am very pleased with the various CPSP surveillance studies that were initiated in 2010: paediatric myasthenia, adrenal suppression, persistent albuminuria in the paediatric population with type 2 diabetes mellitus and respiratory syncytial virus (RSV) infections in paediatric transplant patients.

In 2010, the CPSP also became co-chair of the International Network of Paediatric Surveillance Units. Work has already begun to establish closer links with like organizations, such as ORPHANET and the National Organization for Rare Diseases (NORD), and to emphasize the importance of rare diseases surveillance through various activities.

I would particularly like to highlight the CPSP's dedication to providing ongoing feedback to participants through the CPSP Highlights published in *Paediatrics & Child Health*, CPS News articles, educational resources, ADR Tips of the Month and communications posters.

Collaboration can provide vital information on rare paediatric diseases that can make a difference in the life of an affected child, and inform clinicians and the public alike.

Thanks to everyone for your important contribution.



Dr. Robert Hilliard

CPSP Chair

In the fall of 2010, I was pleased to accept the position of Chair of the Canadian Paediatric Surveillance Program Steering Committee, after serving on the committee in various capacities for four years. I would like to take this opportunity to thank my predecessor, Dr. Lonnie Zwaigenbaum from Edmonton, Alberta, for his excellent work on the Steering Committee and to wish him the best in his future endeavours. The Steering Committee also said goodbye to Dr. Bryce Larke from Edmonton, Alberta, who dedicated many years to the program, and Dr. Catherine McCourt from the Public Health Agency of Canada. Two new committee members were welcomed: Dr. Paul Thiessen from Vancouver, British Columbia and Dr. Claude Cyr from Sherbrooke, Quebec.



Dr. Kimberly Dow

Over the past year, the Steering Committee has been diligently reviewing many interesting proposals in different areas, such as mental health and genetics, to name a few. We look forward to the range of studies that will unfold in the coming year and working alongside such dedicated research teams. I encourage you to take note of the final study findings on bulimic eating disorders, congenital myotonic dystrophy, methicillin-resistant *Staphylococcus aureus* in hospitalized children, serious adverse events associated with paediatric complementary and alternative medicine, and severe combined immunodeficiency.

Committee members have also been active in strengthening and implementing new administrative policies, and in reviewing work plans and progress reports to offer a robust electronic reporting system to participants in 2011.

Finally, I would like to thank the members of the paediatric community for their continued participation and engagement in the CPSP. I would also like to highlight the important support and collaboration the program receives from the Public Health Agency of Canada. By working together, we can create a better life for children and youth living with rare diseases and conditions.

CPSP Steering Committee

Kimberly Dow, MD (incoming Chair)	Canadian Paediatric Society
Lonnie Zwaigenbaum, MD (outgoing Chair)	Canadian Paediatric Society
Claude Cyr, MD	Canadian Paediatric Society
Denis Daneman, MD	Paediatric Chairs of Canada
Marie Adèle Davis, MBA	Canadian Paediatric Society
Kevin Gordon, MD	Canadian Association of Child Neurology (Liaison)
Danielle Grenier, MD	Canadian Paediatric Society
W. James King, MD	Canadian Paediatric Society
Melanie Laffin Thibodeau, BCom	Canadian Paediatric Society
Bryce Larke, MD	Canadian Paediatric Society
Catherine McCourt, MD	Centre for Chronic Disease Prevention and Control, Public Health Agency of Canada
Dorothy Moore, MD	IMPACT (Immunization Monitoring Program ACTive) (Liaison)
Paul Muirhead, LL.M.	Consultant
Jeff Scott, MD	Canadian Paediatric Society
Paul Thiessen, MD	Canadian Paediatric Society
Lesley Ann Turner, MD	Canadian College of Medical Geneticists (Liaison)
Anne-Marie Ugnat, PhD	Centre for Chronic Disease Prevention and Control, Public Health Agency of Canada
Tom Wong, MD	Centre for Communicable Diseases and Infection Control, Public Health Agency of Canada
Sandra Woods, MD	Canadian Paediatric Society

In 2010, **Lonnie Zwaigenbaum**, **Bryce Larke**, and **Catherine McCourt** completed their term as members of the CPSP Steering Committee. We thank them all for their dedication and commitment to the program and wish them the best in future projects.

CPSP Working Group

Melanie Laffin Thibodeau, BCom (Chair)	Canadian Paediatric Society
Marie Adèle Davis, MBA	Canadian Paediatric Society
Laurence Gillieson, BA	Canadian Paediatric Society
Danielle Grenier, MD	Canadian Paediatric Society
Anne-Marie Ugnat, PhD	Centre for Chronic Disease Prevention and Control, Public Health Agency of Canada

Publications 2006-2010



Published papers related to studies

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

Acquired demyelinating syndromes of the CNS

Incidence of acquired demyelination of the CNS in Canadian children. Banwell B, Kennedy J, Sadovnick 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

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, Laeeque H. *Paediatr Child Health* 2009; 14(6): 385-7

Congenital myotonic dystrophy

Congenital myotonic dystrophy in a national registry. Prendergast P, Magalhaes S, Campbell C. *Paediatr Child Health* 2010; 15(8): 514-8

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

Kernicterus / neonatal hyperbilirubinemia

Acute neurological findings in a national cohort of neonates with severe neonatal hyperbilirubinemia. Sgro M, Campbell D, Barozzino T, Shah V. *J Perinatol advance online publication*, December 9, 2010; doi:10.1038/jp.2010.137

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 infection

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

Non-type 1 diabetes mellitus

Type 2 diabetes, medication-induced diabetes, and monogenic diabetes in Canadian children: A prospective national surveillance study. Amed S, Dean HJ, Panagiotopoulos C, Sellers EAC, Hadjiyanakis S, Laubscher TA, Dannenbaum D, Shah BR, Booth GL, Hamilton JK. *Diabetes Care* 2010; 33(4): 786-91

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 2010 in *Paediatrics & Child Health*

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

CPSP 2010 Quiz – *Paediatr Child Health* 2010; 15(10): 640, 675-7

Baby boy blue: Why is this newborn lethargic? Rieder M, Koren G. *Paediatr Child Health* 2010; 15(9): 571-2

Baby products and injuries in Canada: Is it still an issue? Skinner R, Ugnat A-M, Grenier D. *Paediatr Child Health* 2010; 15(8): 490

Adrenal suppression: An under-recognized complication of a common therapy. Goldbloom EB, Ahmet A. *Paediatr Child Health* 2010; 15(7): 411-2

Renal disease in youth with type 2 diabetes: Need for early detection. Sellers E. *Paediatr Child Health* 2010; 15(5): 256-7

Paediatric myasthenia: A moving target. Kolski H. *Paediatr Child Health* 2010; 15(4): 226

Why is this tachypneic child so pale? Parkin P, Szlotkin S. *Paediatr Child Health* 2010; 15(3): 135-6

Langerhans cell histiocytosis: A complex recurrent disease. Crooks B, Grenier D. *Paediatr Child Health* 2010; 15(2): 69-70

CPSP 2009 Quiz – *Paediatr Child Health* 2010; 15(1): 45-7

Presentations in 2010

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

National

Acute flaccid paralysis

A comparison of the World Health Organization's Quality Assurance Criteria for Acute Flaccid Paralysis Surveillance in Canada to other countries. Helferty M, Mitschke M. Canadian Immunization Conference, Quebec City, in December (poster)

Early-onset eating disorders

Early-onset eating disorders – Not just a “dieting” phase. Katzman D, Pinhas L. Canadian Paediatric Society Annual Conference, Vancouver, in June (oral)

Surveillance – General

Paediatric antiviral drug use during H1N1 – Any cause for concern? Grenier D, Ugnat A-M, Davis MA, Laffin Thibodeau M. Canadian Paediatric Society Annual Conference, Vancouver, in June (poster)

Travel-related illnesses

Travel-related illnesses in Canadian children. Crockett M. Canadian Paediatric Society Annual Conference, Vancouver, in June (poster)

International

Child maltreatment

Head injury secondary to suspected child maltreatment in Canada – Results of a national surveillance program. King WJ. Safety 2010 World Conference, London, in September (oral)

Surveillance – General

Surveillance and beyond: The Canadian experience. Grenier D. International Network of Paediatric Surveillance Units (INoPSU) Conference, Dublin, in October (oral)

Challenges and responses: The Canadian Paediatric Surveillance Program. Ugnat AM. International Network of Paediatric Surveillance Units (INoPSU) Conference, Dublin, in October (oral)

Public health impacts of the International Network of Paediatric Surveillance Units. Grenier D. Irish Paediatric Association Meeting, Dublin, in October (oral)

Surveillance at Work

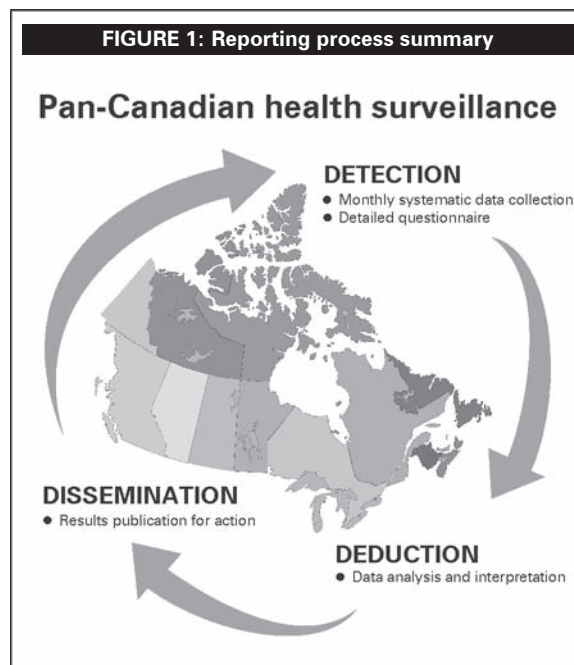
Overview

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 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. If further information is required to confirm or exclude a case, the program senior coordinator contacts the respondent on behalf of the investigator.

TABLE 1
Initial response rates (%)
and number of participants for 2010

Provinces/territories	Reporting rates (%)	Number of participants
Alberta (AB)	78	325
British Columbia (BC)	72	274
Manitoba (MB)	86	117
New Brunswick (NB)	73	33
Newfoundland and Labrador (NL)	88	50
Nova Scotia (NS)	88	102
Northwest Territories (NT)	100	2
Nunavut (NU)	69	3
Ontario (ON)	82	1,009
Prince Edward Island (PE)	85	7
Quebec (QC)	81	611
Saskatchewan (SK)	75	56
Yukon (YT)	100	1
Canada	80	2,590

TABLE 2
2010 detailed questionnaire completion rates
as of May 1, 2011

Studies/conditions	Reported cases*	Pending	% Completion rate
Acute flaccid paralysis	46	0	100
Adrenal suppression	24	3	88
Adverse drug reactions – serious and life-threatening	31	4	87
Bulimic eating disorders	11	1	91
Congenital myotonic dystrophy	1	1	—
Langerhans cell histiocytosis	14	1	93
Methicillin-resistant <i>Staphylococcus aureus</i> in hospitalized children	53	5	91
Paediatric myasthenia	39	0	100
Persistent albuminuria in the paediatric population with type 2 diabetes mellitus	15	0	100
Respiratory syncytial virus (RSV) infections in paediatric transplant patients	1	1	—
Serious adverse events associated with paediatric complementary and alternative medicine	3	2	33
Severe combined immunodeficiency	0	0	—
Severe iron-deficiency anemia in infants and young children	100	25	75
Travel-related illnesses in paediatric travellers who visit friends and relatives abroad	49	8	84
Total number of cases (all studies)	387	51	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 80% national reporting rate (Table 1) and the 87% response rate for completion of detailed questionnaires (Table 2).

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 2010, the majority of participants (88%) had ‘nil’ cases to report. The importance of zero reporting must be re-emphasized. Table 3 illustrates the number of cases reported by respondents in 2010. As studies come and go, the workload shifts to different subspecialties. Through the years, studies with national collaborative networks have been very successful. The 2010 study with the most reports was severe iron-deficiency anemia in infants and young children.

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, names of participants who completed the initial reporting forms for all months in 2010 and/or returned one or more detailed questionnaires were entered in a draw. Drs. Poornima S. Murthy (Saskatchewan) and Michele S. Gingras (British Columbia) 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 2011 CPS Annual Conference in Quebec City were Dr. Marie-Claude Lebeau (Quebec), who responded for all months in 2010, and Dr. Amanda Barclay (British Columbia), who completed and returned a questionnaire for a reported case.

TABLE 3

Number of cases reported by respondents in 2010

Number of cases	Respondents (%)
0	2,382 (88%)
<5	311 (11%)
5-10	12 (0.4%)
>10	1 (0.04%)

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 over 2,500 participants. The program is committed to a high case ascertainment rate 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 for Inclusion, and follow the Format for Submission,

available at www.cps.ca/english/surveillance/CPSP/Investigators. The Steering Committee reviews submissions at its spring and fall meetings, giving preference to studies that have either strong scientific and public health importance or those that could not be undertaken any other way. Following the review, studies must receive ethical approval and have external funding arrangements in place before final acceptance to the program. Researchers interested in obtaining more information about the program are encouraged to visit the website at www.cps.ca/cpsp or contact the CPSP senior coordinator at cpsp@cps.ca.

One-time survey questions

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

Results of the 2010 one-time survey questions are found on pages 55-57.

Survey questions

TABLE 4

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
Baby products injury	February 2010
Patients with asymptomatic adrenal suppression	March 2010
Complications associated with infant male circumcision	December 2010

Studies timeline

TABLE 5
CPSP studies timeline (by end date)

Study	Start date	End date	Total confirmed cases to December 31, 2010
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	38
Bulimic eating disorders	March 2008	February 2010	182
Severe combined immunodeficiency	April 2004	March 2010	44
Methicillin-resistant <i>Staphylococcus aureus</i> in hospitalized children	September 2008	August 2010	171
Serious adverse events associated with paediatric complementary and alternative medicine	January 2009	December 2010	8
Travel-related illnesses in paediatric travellers who visit friends and relatives abroad	March 2009	February 2011	77
Severe iron-deficiency anemia in infants and young children	October 2009	September 2011	18
Paediatric myasthenia	January 2010	December 2011	86
Adrenal suppression	April 2010	March 2012	33
Persistent albuminuria in the paediatric population with type 2 diabetes mellitus	April 2010	March 2012	18
Langerhans cell histiocytosis	July 2009	June 2012	14
Respiratory syncytial virus (RSV) infections in paediatric transplant patients	September 2010	August 2013	0
Acute flaccid paralysis	January 1996	December 2013	657
Adverse drug reactions – serious and life-threatening	January 2004	December 2013	269

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.

CPSP Principal Investigators



Surveillance studies in 2010



Dr. Shalini Desai
Acute flaccid paralysis



Dr. Ellen Goldbloom
Adrenal suppression



Margaret Zimmerman
Adverse drug reactions – serious and life-threatening



Dr. Leora Pinhas
Bulimic eating disorders



Dr. Craig Campbell
Congenital myotonic dystrophy



Dr. Bruce Crooks
Langerhans cell histiocytosis



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



Dr. Hanna Kolski
Paediatric myasthenia



Dr. Elizabeth Sellers
Persistent albuminuria in the paediatric population with type 2 diabetes mellitus



Dr. Joan Robinson
Respiratory syncytial virus (RSV) infections in paediatric transplant patients



Dr. Sunita Vohra
Serious adverse events associated with paediatric complementary and alternative medicine



Dr. RoseMarie Ramsingh
Severe combined immunodeficiency



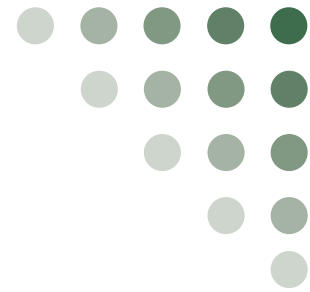
Dr. Patricia Parkin
Severe iron-deficiency anemia in infants and young children



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



Surveillance Studies in 2010



Acute flaccid paralysis

January 1996 to December 2013

Highlights 2010

- 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 95% of all AFP cases.
- Guillain-Barré syndrome continues to be the most frequent diagnosis for AFP in Canada.
- Canada's AFP surveillance continues to work towards the World Health Organization (WHO) targets for AFP detection, stool specimen collection and follow-up for residual paralysis.

Background

Elimination of indigenous wild poliovirus transmission was certified in Canada in September 1994, along with the rest of the Region of the Americas (North, South and Central America). However, until global eradication of poliomyelitis is achieved, there remains an ongoing risk for importation of wild polioviruses. In 2010, endemic circulation of wild poliovirus continued in four countries: Afghanistan, India, Nigeria and Pakistan. There were 920 cases of wild poliovirus reported from a total of 30 countries worldwide as compared with 1,604 cases in 2009 (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 WHO quality assurance criteria include:

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

Case definition

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

Results

There were 52 notifications of AFP through the CPSP to the Public Health Agency of Canada with onset in 2010, which included 38 confirmed cases (Table 6). Case ascertainment for all confirmed cases in 2010 occurred in equal proportion between IMPACT sites and the CPSP. In addition, there

was a higher proportion (74%) of confirmed cases reported from Ontario and Quebec. The remaining confirmed cases were reported from Western Canada (24%) 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.

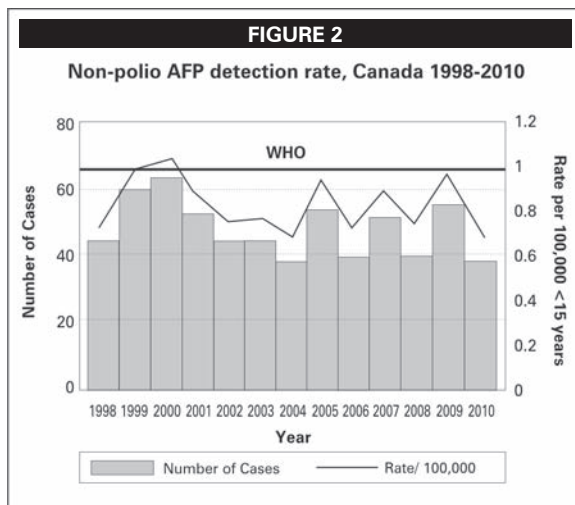
TABLE 6

AFP cases in 2010

Reported	Duplicates	Excluded	Pending	Confirmed
52	8	3	3	38

Eleven AFP reports were excluded: three based on age criteria and eight were duplicates. The 38 confirmed cases in 2010 represent a non-polio AFP detection rate of 0.68/100,000 in children less than 15 years of age (Figure 2) which does not meet the 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 the reporting calendar year.

Of note, Figure 2 has recently been revised as a result of an evaluation of the AFP database. Through this process a number of improperly coded cases were identified. The most notable change resulting from this review is that the non-polio AFP rate was not met in 2009 as previously reported.



In 2010, AFP cases ranged in age from two weeks to 14 years (median 9 years, mean 8 years) and

were fairly evenly distributed across the age groups. Similar to last year's results, the majority (61%) of AFP cases were reported in males as compared to females.

Documentation of age-appropriate polio immunization remains incomplete; only 15 (39%) cases had documented receipt, nine (24%) were reported as "up-to-date" but with no accompanying details, and the remaining 14 (37%) included no information. Of note, vaccine uptake rates of IPV in Canada have been consistently high (95% uptake for three doses).

Investigation for polio virus, other enteroviruses or Campylobacter

Virological investigation included collection and testing of stool specimens for 17 cases (45%), cerebrospinal fluid (CSF) for 25 cases (66%) and throat swabs for 13 cases (34%). Where stool was collected, 88% 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. Over the course of this study, the proportion of adequate stool samples collected within 14 days of the onset of paralysis in Canada has averaged at 32% and has never met the WHO surveillance target of 80%. In 2010 the proportion was above the Canadian average at 39%. There was no positive identification of polioviruses from any of the virological investigations in 2010. Testing was also conducted for *Campylobacter* in 16 (42%) cases and was not isolated in any of the samples.

Neurological investigations

In 2010, approximately 97% 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 (89%). Of these, approximately 62% had abnormal CSF chemistry results, 62% abnormal EMG and/or nerve conduction studies and 38% abnormal MRI or CT scans.

As observed in previous years, the majority of AFP cases (n=29, 76%) were GBS, three of which were Miller-Fisher variant. The remaining nine diagnoses

included transverse myelitis (n=4), Bell's palsy (n=2), acute disseminated encephalomyelitis (n=1) and other (n=2).

Hospitalization and outcome

All confirmed AFP cases reported in 2010 required hospitalization, with lengths of stay ranging from one to 90 days (median 11 days, mean 15 days). For one case, the length of stay was unknown. Outcome at the time of the initial report was documented in 32 cases (84%): seven (18%) fully recovered, 20 (53%) partially recovered with residual weakness or paralysis, and five (13%) had not fully recovered but were reported to be improving. There were no deaths. Only 18 cases (47%) had clinical status at 60 days reported, including: seven cases who had fully recovered; seven with partial recovery, some residual weakness or paralysis; and four 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 38 AFP cases were confirmed in 2010, giving a national non-polio AFP detection rate of 0.68 case per 100,000 population in children less than 15 years of age, which does not meet the WHO's quality assurance criteria. The recommended target has only been met twice (in 1999 and 2000) since AFP surveillance began in 1996. 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. This lower baseline level has been observed in other developed nations, and is worthy of further exploration with WHO to determine appropriate performance indicators for developed nations.

The majority of cases of poliomyelitis are asymptomatic; a small percentage of cases, approximately 4–8%, may manifest as a non-specific fever and sore throat. Approximately 1% of cases develop paralytic poliomyelitis. Symptoms of this form of polio include severe muscle pain and stiffness of the back and neck; rapid onset

of asymmetric acute flaccid paralysis may occur. There is usually a fever present at the onset of illness and the paralysis depends on the location of nerve cell infection. If poliomyelitis is suspected in a patient, further consultation with a neurologist and infectious diseases consultant would be prudent.

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. The data that is received can be improved by 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. Other plans for the future include: improving the data collection form, evaluating the functionality of the AFP surveillance systems and investigating ways of supplementing the AFP data system.

Global Polio Eradication Initiative (GPEI) www.polioeradication.org

In 2010, while just over 1,292 cases of poliomyelitis were reported globally, only 18% of these occurred in the four countries where indigenous polio transmission is still occurring: Nigeria, India, Pakistan and Afghanistan. This is different than in previous years where the majority of cases occurred in endemic countries (i.e., in 2009, 78% of cases were from endemic countries). Large outbreaks of polio in Tajikistan and the Republic of Congo account for 65% of the cases in 2010,

with an additional five countries reporting cases of reintroduction of poliovirus. This serves as an important reminder of the possibility of importation, especially in countries like Canada that have been polio-free for many years. While polio eradication has faced some challenges, in 2010 the GPEI announced its strategic plan for the next three years. The plan is an aggressive, time-bound work plan, with ongoing evaluation, to interrupt transmission of wild poliovirus from the remaining reservoirs internationally by 2013.

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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Publications and presentations

Helferty M, Mitschke M. A comparison of the World Health Organization's Quality Assurance Criteria for Acute Flaccid Paralysis Surveillance in Canada to Other Countries. Canadian Immunization Conference, Quebec City, December. (Poster presentation)



Adrenal Suppression

April 2010 to March 2012

Highlights 2010

- In the first nine months of surveillance, 18 cases of symptomatic AS were confirmed.
- Adrenal crisis, a condition with significant morbidity, was confirmed in three cases.
- Growth failure was the most common presenting sign in children with AS.
- The majority of cases of AS were seen in boys.
- The predominant type of glucocorticoid (GC) treatment in most of the cases reported was inhaled corticosteroids. Many were treated with more than one form of GC (e.g., inhaled and intranasal).
- There were no reported cases of AS for children being treated with intranasal GCs alone.

Background

Glucocorticoid (GC) therapy is used in the treatment of several paediatric diseases. While the efficacy of GCs has been well established, there can be potentially serious side effects. Among them is adrenal suppression (AS) which results in an inability to produce adequate amounts of cortisol – a critical hormone during physiologic stress. AS may go undetected until an illness or other stress precipitates a critical condition known as “adrenal crisis.” Children with adrenal crisis may have critically low blood sugars and/or blood pressure leading to seizure, coma or even death. This can be prevented by recognizing children at risk and administering higher doses of GCs during times of stress. The incidence of AS is unknown. The objective of this study is to estimate the incidence, clinical features and burden of illness of symptomatic AS in the Canadian paediatric population.

Objectives

- 1) Estimate the national incidence of paediatric adrenal crisis and symptomatic adrenal insufficiency due to AS in association with GC treatment, diagnosed by Canadian paediatricians
- 2) Describe the clinical features of AS at diagnosis and document burden of illness
- 3) Identify characteristics of children with symptomatic AS
- 4) Generate awareness among paediatricians of the frequency of AS and associated morbidity in children on GC therapy

Case definition

Report any new patient less than 18 years of age treated with any form of GC therapy with evidence of adrenal suppression defined as:

- Adrenal crisis, an acute critical illness out of proportion in severity to the current illness and manifested by any of the following:
 - Hypotension/shock
 - Decreased level of consciousness/lethargy
 - Unexplained hypoglycemia or hyponatremia
 - Seizure
 - Death

OR

- Symptomatic* adrenal insufficiency with supportive biochemical evidence

* Signs/symptoms can include anorexia, weakness, fatigue, lethargy, fever, gastrointestinal symptoms (nausea, vomiting, constipation, diarrhea, abdominal pain), morning headache, hypoglycemia, myalgia, arthralgia, psychiatric symptoms and growth failure.

Exclusion criteria

Adrenal insufficiency unrelated to GC therapy, including adrenocorticotropic hormone (ACTH) deficiency due to hypothalamic or pituitary gland abnormalities, and primary adrenal disorders, such as:

- Congenital adrenal hyperplasia
- Autoimmune adrenalitis or polyglandular syndromes
- Adrenal hypoplasia congenita
- ACTH resistance syndromes
- Metabolic disorders (adrenoleukodystrophy, peroxisome biogenesis disorders, cholesterol metabolism, mitochondrial disorders)

- Infectious disorders (sepsis, tuberculosis, fungal infections, viral infections)
- Infiltrative/destructive causes (hemorrhage, amyloidosis, sarcoidosis, metastases)
- Drugs inhibiting steroid biosynthesis (e.g., ketoconazole, etomidate, suramin, aminoglutethimide, metyrapone)

Results

TABLE 7

AS cases from April 1 to December 31, 2010

Reported	Duplicates	Excluded	Pending	Confirmed
39	3	8	10	18

Demographics

In the first nine months of surveillance, 18 cases of symptomatic AS were confirmed. Fourteen (78%) were male. The mean age at diagnosis of AS was 10.8 years (range 4.5–18). The vast majority were Caucasian (n=16, 89%), one (5%) was Asian and one (5%) was reported as “other” for ethnicity. The underlying conditions requiring GC treatment included asthma alone (n=11, 61%), asthma and atopy (n=2, 11%), inflammatory bowel disease and arthritis (n=1, 6%), malignancy (n=2, 11%), and eosinophilic esophagitis (n=2, 11%). Seven cases (39%) were from Quebec, nine (50%) were from Ontario and two (11%) were from British Columbia. The confirmed cases presented to a physician’s office or clinic (n=13, 72%), to the emergency department (n=2, 11%), on the inpatient unit (n=2, 11%) and in the paediatric intensive care unit (n=1, 6%).

Glucocorticoid therapy

Twelve children received inhaled corticosteroids (ICS) in solo therapy (n=5) or in combination with a short course oral GC (n=3), intranasal GC (n=2), and intranasal and short course oral GC (n=2). Two children with a diagnosis of eosinophilic esophagitis were treated with topical ICS. In this scenario, glucocorticoid therapy is given topically to the esophagus by swallowing budesonide suspension or inhaling fluticasone into the mouth (without a spacer) and then swallowing water. One of these children received ICS as well. Four children received primarily systemic GCs: intravenous only (n=1), oral only (n=1), and a

combination of intravenous and oral GCs (n=2). The specific types, doses and treatment durations of GCs were variable and were not consistently reported. The most commonly reported ICS was fluticasone usually in doses of 250 to 500 mcg/day for months to years.

Presentation

Of the 18 confirmed cases of symptomatic AS, the most common presenting sign was growth failure. Three cases (17%) had adrenal crisis. The presenting symptoms and signs of the remaining cases are described in Table 8.

TABLE 8

Presenting symptoms and signs

	Number of cases (%)
Adrenal crisis	3 (17)
Growth failure alone	9 (50)
Growth failure and non-specific symptoms*	3 (17)
Non-specific symptoms	2 (11)
Hypoglycemia	1 (6)

* Non-specific symptoms included one or more of fatigue, lethargy, weakness, nausea, anorexia, vomiting, abdominal pain, myalgia or arthralgia.

Physical activity

The underlying condition requiring GC therapy caused a decrease in physical activity in four children (22%). The GC therapy caused a decrease in physical activity in two children (11%). Three children (17%) experienced a weight gain on GC therapy.

Outcome and management

After confirmation of AS, eight children (44%) were treated with GC replacement and 13 (72%) were seen by or referred to an endocrinologist. Three children (17%) were hospitalized (all three had adrenal crisis). The remainder (n=15, 83%) were managed as outpatients.

Conclusion

Based on these preliminary results, the minimal estimated incidence of symptomatic AS is approximately 24 cases per year in the Canadian paediatric population. A large proportion of patients had growth failure (either alone or with non-specific symptoms) as their presenting sign.

This underlies the importance of close monitoring of children's growth in the primary care setting – particularly for those treated with GCs. Adrenal crisis at presentation is rare but potentially preventable. The lack of consistent specific symptomatology for AS may suggest that many cases are not recognized without proactive screening of those at risk. Data collected to date do not suggest a large burden of illness but the burden may be more than documented given the likelihood of missed diagnoses and, therefore, under reporting.

Most of the cases reported were boys, suggesting that boys may be more susceptible to AS than girls. Alternatively, the male predominance may simply be due to a gender bias in recognition and assessment of short stature. Boys and their parents are usually more concerned about short stature/poor growth than girls due to increased psychosocial stigmatization of short boys compared to short girls.

While systemic (i.e., intravenous or oral) GCs are often perceived as being the most suppressive, the majority of the reported cases were in the setting of ICS which is consistent with the existing paediatric literature. These children received commonly prescribed (albeit high) doses of ICS. Due to the high prevalence of asthma in the Canadian paediatric population, ICSs are commonly prescribed. Therefore, it is important to understand the risks associated with this treatment. Many of the reported cases were treated with GCs given by more than one route, suggesting the importance of consideration of the cumulative GC dose when assessing a child's risk for AS. It remains unclear what dose of GC is required to cause AS; however, to date, none of the children reported in our study have received low doses of ICS (e.g., less than 500 mcg/day of fluticasone) alone. Despite the relative rarity of eosinophilic esophagitis (which responds to treatment with swallowed topical GC), it is interesting that two of the 18 cases reported had this diagnosis. Children treated with this type and route of GC may be particularly susceptible to AS.

Given the morbidity associated with AS and the potential for intervention and treatment of those

affected, it is crucial to understand which children are at risk of this serious complication of GC therapy. National surveillance of AS in Canadian children will help describe the associated morbidity and provide data for future development of screening, prevention and treatment guidelines. Screening guidelines will be particularly important in identifying and treating children with AS prior to the development of symptoms or adrenal crisis. In the setting of asthma management, an approach to detection and treatment of AS in children may improve outcomes. The implementation of screening guidelines will prevent morbidity, mortality and costly hospitalizations in our paediatric population.

Over the past year, the CPSP study has provided an ideal format for data collection to estimate the frequency and morbidity of this condition in Canada. It has also been an effective tool in raising awareness about this condition and in contributing to the recognition of children at risk of AS.

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Adverse drug reactions – serious and life-threatening

January 2004 to December 2013

Highlights 2010

- In 2010, 32 cases of suspected paediatric adverse reaction (AR) reports were confirmed.
- Product groups most commonly associated with suspected adverse reactions were antibacterial, psychoanaleptic and psycholeptic agents.
- Reactions from System Organ Class psychiatric disorders have increased from 2.5% in 2008 to 17.6% in 2010.
- Approximately one-third of the AR reports also described dermatological manifestations.

Background

Adverse drug reactions (ADRs) are an important cause of illness and death. Of particular concern is the alarming lack of understanding of the extent and causes of ADRs in the paediatric population and, therefore, the limited ability to avoid or prevent these occurrences. Children are not small adults and are known to be at greater risk related to a host of biological, developmental and behavioural factors affecting the safety and effectiveness of pharmaceuticals.

A three-year study evaluating paediatric AR reports collected through the Canadian Paediatric Surveillance Program (CPSP) was undertaken in 2003–2006. Since January 1, 2007, the collection of reports of serious and life-threatening ARs has continued through the CPSP and includes submission of completed AR reports to the Canada Vigilance Program. The Canada Vigilance Program of the Marketed Health Products Directorate (MHPD) of Health Canada is responsible for collecting and assessing AR reports for the following health products marketed in Canada: pharmaceuticals, biologicals, natural health products and radiopharmaceuticals. The information collected in Canadian AR reports is entered and maintained in a computerized database and is used for the monitoring of marketed health products.

Objectives

- 1) Continue the reporting and monitoring of serious and life-threatening adverse reactions collected through the CPSP

- 2) Identify products most frequently causing ADRs in children, the type of reactions encountered and the characteristics of those affected

Case definition

Report serious and life-threatening adverse 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.

* Noxious and unintended severe response to a health product, 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 9

Serious and life-threatening ADR cases in 2010

Reported	Duplicate	Excluded	Pending	Confirmed
42	0	2	8	32

From January 1 to December 31, 2010, 42 cases of suspected serious ADRs were reported and 32 confirmed cases were submitted to the Canada Vigilance Program through the CPSP. In comparison, 51, 40 and 45 AR reports were received via the CPSP in 2009, 2008 and 2007 respectively.

Of the 32 confirmed cases, 17 were male, 13 were female and in two cases the sex of the patient was not provided. The age range was from two months to 17 years. Table 10 provides a comparison of the age distribution of AR reports received in the past three years.

TABLE 10

Annual comparison of age distribution

	2010 (n=32)	2009* (n=51)	2008† (n=40)	2007 (n=45)
Up to 5 years of age	6	14	15	9
6 to 12 years	15	16	14	16
13 to 17 years	10	21	11	18
Not reported	1	0	0	2

* The 2009 number of cases has been adjusted to reflect delayed reports not included in the *CPSP 2009 Results*.

† The 2008 number of cases has been adjusted to reflect delayed reports not included in the *CPSP 2008 Results*.

All 32 cases were classified as serious (more than one reason for seriousness was reported in 11 reports). Table 11 shows a comparison of the reasons for seriousness of the AR reports received in the past four years.

TABLE 11

Annual comparison of reasons for seriousness

	2010 (n=32)	2009 (n=45)	2008 (n=35)	2007 (n=41)
Death	0	1	3	0
Life-threatening	6	14	12	9
Hospitalization	19	28	18	19
Disability	2	3	0	0
Medically important condition*	17	21	12	11

* 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 30 of the 32 reports as follows: recovered (n=30); not yet recovered (n=1); recovered with sequelae (n=1).

All reports described reactions that were documented in standard drug reference sources for the health product except for three: (1) hypertriglyceridaemia with pancreatitis in a diabetic patient treated with oseltamivir for influenza-like

illness; (2) small pericardial effusion associated with amoxicillin used for the treatment of scarlet fever; (3) hyperammonaemic encephalopathy associated with cisplatin and fluorouracil for the treatment of metastatic hepatocellular carcinoma. It was not possible to confirm the documentation of the reactions in standard drug references for one report where the suspect product was an unspecified Benylin[®] product and the active ingredients could not be identified. The information source used to make these determinations was the Canadian-approved product monograph. When an approved product monograph was not available, the source used was the Compendium of Pharmaceuticals and Specialties, electronic version, the Micromedex[®] Drug Information System or the American Hospital Formulary Service[®] (AHFS) Drug Information reference. It should be noted that adverse reaction reports are suspected associations which reflect the opinion or observation of the individual reporter. Certain reported reactions may occur spontaneously and occur as a background rate in the general population. The reported reaction may have a temporal, but not necessarily a causal, relationship with the health product.

Suspected health products

Table 12 lists all suspect health products named in the 32 AR reports, sorted by the number of reports received for each individual product. In 25 reports, a single product was suspected of causing the reaction(s). Two suspect products were reported in four cases, three suspect products in two cases, and five suspect products in one case. The class of health products most frequently suspected of causing the adverse reaction(s) was antibacterial agents (n=8). Next in frequency was psychoanaleptics (n=7; five cases with psychostimulant agents used for the treatment of attention deficit and hyperactivity disorders and two with antidepressants), followed by psycholeptic agents (n=4). These findings differ from previous years when reports for anti-epileptic and anti-neoplastic agents were among the three most frequently reported suspect products. Of note, the occurrence of reactions from System Organ Class psychiatric disorders of the Medical Dictionary for Regulatory Activities (MedDRA[™]) has increased from 2.5% in 2008, to 11.8% in 2009 and to 17.6% in 2010.

TABLE 12

Suspected health products reported in AR reports (n=32) in 2010

Suspected health product	# Time reported (n=44)
Methylphenidate hydrochloride, immediate and extended release*	5 (n=5)
Amoxicillin	3 (n=3)
Prednisone, valproic acid†	2 each (n=4)
Arginine, atomoxetine, azithromycin, unspecified Benylin® product, cefazolin, cisplatin, clindamycin, dexamethasone, ethambutol, fluorouracil, fluoxetine, fluticasone/salmeterol‡, haloperidol, immunoglobulin (human), levetiracetam, lidocaine (topical), metoclopramide, naproxen, oseltamivir, phenytoin, probenecid, prochlorperazine, pyrazinamide, rifampin, risperidone, salbutamol, sevoflurane, succinylcholine, sulfamethoxazole/trimethoprim‡, sulfasalazine, tretinoin, ziprasidone	1 each (n=32)

* Includes three different brands (Concerta®, Ritalin®, Biphentin®)

† Includes valproic acid as divalproex sodium and as sodium valproate

‡ Combination products containing two active ingredients

Conclusion

The class of health products most frequently suspected of causing adverse reactions was antibacterial agents (n=8). Next in frequency was psychoanaleptics (n=7: five cases with psychostimulant agents used for the treatment of attention deficit and hyperactivity disorders (ADHD) and two with antidepressants followed

by psycholeptic agents (n=4). Of note, during the period of the study, the Canadian Paediatric Society released a guideline on the use of extended-release medications for children and adolescents with ADHD. All these classes of health products are frequently used in paediatric care. Approximately one-third of the AR reports also described dermatological manifestations.

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

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

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APPENDIX 1

Summary of 32 adverse reaction reports reported to the Canada Vigilance Program through the Canadian Paediatric Surveillance Program (CPSP), January 1 to December 31, 2010

Age	Suspect product(s)	Indication for use	Reaction(s)*	Seriousness	Outcome†
10 y	Sulfamethoxazole-trimethoprim	Urinary tract infection	Stevens-Johnson syndrome Toxic epidermal necrolysis Dermatitis bullous	Life-threatening Hospitalization Medically important	Recovered with sequelae
12 y	Methylphenidate, extended release Valproic acid Atomoxetine	Attention deficit hyperactivity disorder Bipolar disorder	Nausea, vomiting Hepatitis Alanine aminotransferase increased Aspartate aminotransferase increased Blood albumin decreased International normalised ratio abnormal	Hospitalization Medically important	Recovered
13 y	Amoxicillin	Scarlet fever	Pericardial effusion Urticaria	Medically important	Recovered
14 y	Tretinoin	Acute myelogenous leukaemia	Pharyngeal inflammation	Life-threatening Hospitalization	Recovered

APPENDIX 1 (cont`d)

Age	Suspect product(s)	Indication for use	Reaction(s)*	Seriousness	Outcome†
16 y	Oseltamivir	Influenza-like illness	Abdominal pain Pancreatitis Hypertriglyceridaemia Blood amylase increased Lipase increased	Hospitalization Medically important	Recovered
9 y	Zispridone	Not provided	Delirium Facial spasm Oculogyric crisis	Disability Hospitalization	Recovered
11 y	Cisplatin Fluorouracil	Metastatic hepatocellular carcinoma	Hyperammonaemic encephalopathy Visual impairment	Hospitalization	Recovered
5 y	Fluticasone-salmeterol	Asthma	Adrenal insufficiency Blood cortisol decreased	Medically important	Not recovered
14 y	Prochlorperazine	Vomiting	Dyskinesia Balance disorder Diplopia Drooling Dysarthria Dystasia Extensor plantar response Muscle spasms Strabismus	Hospitalization	Recovered
1 y	Amoxicillin	Otitis	Angioedema Erythema multiforme Hyponatremia	Hospitalization	Recovered
3 y	Dexamethasone Lidocaine, topical Sevoflurane Succinylcholine Salbutamol	Surgical procedure	Rhabdomyolysis Arthropathy Gait disturbance Alanine aminotransferase increased Aspartate aminotransferase increased Blood creatine phosphokinase increased	Life-threatening Hospitalization	Unknown
13 y	Immunoglobulin, human	Atypical Kawasaki disease	Haemolysis Blood lactate dehydrogenase increased Coombs direct test positive Haemoglobin decreased Haptoglobin decreased	Hospitalization Medically important	Unknown
4 y	Haloperidol	Agitation	Dystonia Extrapyramidal disorder Eye movement disorder Hyperreflexia Muscle spasms Speech disorder Torticollis	Hospitalization	Recovered
1 y	Azithromycin	Tonsillitis	Stevens-Johnson syndrome Lip swelling Mouth ulceration Rash papular	Hospitalization	Recovered
14 y	Arginine	Growth hormone stimulation test	Hyperkalemia	Hospitalization Medically important	Recovered
6 m	Clindamycin injection and oral	Methicillin-resistant <i>Staphylococcus aureus</i>	Neutropenia	Life-threatening	Recovered
15 y	Cefazolin injection Probenecid	Osteomyelitis of the hip	Pruritus Rash erythematous Skin exfoliation	Medically important	Recovered
7 y	Benylin® (not otherwise specified)	Cough, Upper respiratory tract infection	Anxiety Hallucination, auditory Hallucination, visual	Medically important	Recovered

APPENDIX 1 (cont`d)

Age	Suspect product(s)	Indication for use	Reaction(s)*	Seriousness	Outcome†
12 y	Phenytoin	Seizure disorder	Pyrexia, cough Pharyngitis, rhinitis Lymphadenopathy Rash maculo-papular Rash morbilliform Drug rash with eosinophilia and systemic symptoms White blood cell count increased Platelet count decreased Alanine aminotransferase increased Blood alkaline phosphatase increased Gamma-glutamyltransferase increased	Hospitalization	Recovered
12 y	Ethambutol Pyrazinamide Rifampin	Pulmonary tuberculosis	Pyrexia, abdominal pain Rash generalized Hepatitis Renal failure Alanine aminotransferase increased Aspartate aminotransferase increased Blood creatinine increased Blood urea increased Gamma-glutamyltransferase increased	Hospitalization Medically important	Recovered
11 y	Levetiracetam	Convulsion prophylaxis following head trauma	Hepatitis Alanine aminotransferase increased Aspartate aminotransferase increased Gamma-glutamyltransferase increased	Medically important	Recovered
Child	Methylphenidate	Attention deficit hyperactivity disorder	Psychotic disorder	Medically important	Recovered
13 y	Methylphenidate, extended release	Attention deficit hyperactivity disorder	Hallucination, auditory Psychotic disorder	Medically important	Recovered
17 y	Fluoxetine	Depression	Akathisia	Disability	Recovered
8 y	Methylphenidate, extended release	Attention deficit hyperactivity disorder	Hallucination, visual Psychotic disorder	Medically important	Recovered
15 y	Prednisone Sulfasalazine	Ulcerative colitis	Febrile neutropenia	Hospitalization	Recovered
2 m	Metoclopramide	Gastroesophageal dysmotility	Dyskinesia Irritability Poor quality sleep	Medically important	Recovered
11 y	Risperidone	Developmental problems	Prolonged QT on electrocardiogram	Medically important	Recovered
7 y	Methylphenidate, extended release	Attention deficit hyperactivity disorder	Hallucination	Hospitalization	Recovered
7 y	Valproic acid	Epilepsy	Toxic epidermal necrolysis	Life-threatening Hospitalization	Recovered
6 y	Naproxen Prednisone	Juvenile idiopathic arthritis	Abdominal sepsis Duodenal ulcer with perforation	Life-threatening Hospitalization	Recovered
7 y	Amoxicillin	Acute sinusitis	Pyrexia Urticaria Serum sickness Polyarthrits Red blood cell sedimentation rate increased	Medically important	Recovered

* Terms are listed according to MedDRA v13.1 Preferred term (PT)

† At the time of reporting as indicated by the reporter

Bulimic eating disorders

March 2008 to February 2010 – Final report

Highlights

- Two years of BED surveillance confirmed 182 new cases in children aged five to 18 years.
- BED was commonly identified in adolescent years; 75% of cases were between the ages of 16 and 18 years of age.
- Of the confirmed cases, 91% were receiving regular medical monitoring.
- Inpatient/day hospital management was needed in almost half (n= 66/182, 36%) of cases.
- The most common (64%) mental health intervention was individual therapy.

Background

Little is known about bingeing and purging disorders in young people. Bulimia nervosa (BN) occurs in 1% of the adolescent population with partial symptoms occurring in 3–6%. Mortality rates range from 0–6%. Alarmingly, only 4% of adolescent girls with bingeing and 6% of girls with purging report 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 BN in children are identical to those for adults, although there is evidence that children may differ significantly in their presentation.

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

Objectives

- 1) Determine a conservative incidence rate of children and young adolescents presenting to paediatricians with bulimic eating symptoms and behaviours
- 2) Describe the bulimic behaviours and the associated physical symptoms in children and adolescents on presentation to a paediatrician

- 3) Identify psychiatric co-morbid disorders that accompany bulimic eating disorders (BED)
- 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 old (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 13

BED cases from March 1, 2008 to February 28, 2010

Year	Reported	Duplicates	Excluded	Pending	Confirmed
2008*	116	4	4	8	100
2009	90	2	2	15	71
2010†	14	0	2	1	11
Total	220	6	8	24	182

* March 1 to December 31, 2008

† January 1 to February 28, 2010

In the two-year study period, 182 cases were identified. The mean age at presentation was 16.1 ± 1.31 years (range 12–18 years). Forty-six cases (25%) were under the age of 16 years. Eleven cases (6%) identified were males and the only significant finding related to sex was that males comprised a larger proportion of the visible minority population as opposed to the Caucasian population (21% vs. 4%, $p=0.0001$). Ethnic groups identified in this patient population were Caucasian ($n=144$, 79%), First Nation/Innu/Inuit/Métis ($n=4$, 2%), Asian ($n=14$, 8%), Latin American ($n=5$, 3%) and Middle Eastern ($n=4$, 2%). The remaining cases were missing data or were listed as other.

Both bingeing and vomiting were found in 119 (65%) of the cases. The breakdown of symptoms can be found in Table 14.

Symptom	Frequency (%)
Bingeing	135 (74%)
Vomiting	161 (89%)
Bingeing and vomiting	119 (65%)
Laxative abuse	32 (18%)
Diuretic abuse	5 (3%)
Other weight loss medication	35 (19%)
Exercise	126 (69%)
Food avoidance	152 (84%)
Fear of weight gain	171 (94%)
Preoccupation with food	165 (91%)
Preoccupation with body weight	167 (92%)
Perception that body is larger than it is	127 (70%)
Denial of severity of symptoms	82 (45%)
Somatic complaints	81 (45%)

The mean duration of present illness was 15.3 months (± 12.1 months). Both the median and the mode were 12 months; 39 subjects (21%) had a duration of illness of one year. There was a second peak at 24 months; 25 subjects (14%) had a duration of illness of two years. Roughly one-third of the patients presented within six months or less, one-third within six months to one year, and one-third reported duration of illness to be one to five years. In the previous six months prior to presentation, weight loss was reported in 84 cases (46%), with a mean loss of 10.2 kg (range 1–30 kg), while weight gain was reported in 53 cases (29%), with a mean gain of 7.5 kg (range 1–25 kg).

Of the confirmed cases, 120 children and adolescents (70%) presented with at least one physical symptom. A breakdown of the physical symptoms can be found in Table 15.

Symptom	Frequency (%)
Bradycardia	24 (13%)
Tachycardia	14 (8%)
Hypokalemia	14 (7%)
Dehydration	25 (14%)
Dizziness/syncope	85 (47%)
Decreased gastric motility	37 (20%)
Gastro-oesophageal reflux	31 (17%)
Blood in vomit	24 (13%)

Seventy cases (39%) had at least one gastro-intestinal (GI) symptom, and 28 patients (15%) had two or more GI symptoms. Patients who reported vomiting were more likely to present with a GI complaint (42% with vomiting vs. 12% without, $p=0.016$) and specifically, they were more likely to have decreased gut motility (26% vs. 6%, $p=0.044$). All of the patients who were diagnosed with dehydration were also reported to vomit ($p=0.048$). The majority of patients (95%) who reported vomiting did not have Russell's sign (callus on dorsum of hand). Forty-one patients (23%) had an arrhythmia and 21 cases (12%) had at least one electrolyte abnormality (hypokalemia was most common at 7% of the population (Table 15)). Of the patients that had an electrolyte disturbance, the majority (91%) both binged and vomited.

More than half of the children and adolescents ($n=110$, 60%) had a concurrent comorbid mental health diagnosis and while 62 subjects (34%) had one comorbid diagnosis, 48 subjects (26%) had two or more diagnoses. The most common comorbid disorder was depression ($n=91$, 50%). Seventy-six subjects (42%) had a history of a mental health disorder other than bulimia or binge eating and only 59 subjects (32%) had neither a past nor a concurrent comorbid mental health disorder. Seventy-seven subjects (43%) had at least one family member with a history of a mental health disorder with 49 cases (27%) having a family history of an eating disorder and 64 cases (35%) having a family history of depression. Subjects with a

concurrent depression were more likely to present with somatic complaints (53% vs. 39%, $p=0.039$) as were subjects with a family history of depression (59% vs. 36%, $p=0.006$)

A history of abuse was reported in 37 (20%) cases with 14 (8%) reported to have experienced sexual abuse. Fifty-three subjects (29%) had a history of self-harm and 35 subjects (19%) had a history of suicidal ideation or behaviour. All the children and adolescents who had experienced sexual abuse ($n=13$) were reported to binge eat ($p=0.043$) and binge eating was associated with multiple sex partners. All cases (19 cases, 15% of binge eaters) who had multiple sex partners were reported to binge eat ($p=0.013$). Bingeing was also associated with both sexual abuse and multiple sex partners (87% vs. 73%, $p=0.051$). Vomiting was not associated with sexual abuse, sexual activity or multiple sex partners.

Caucasian subjects were younger (16.0 ± 1.35 years vs. 16.6 ± 0.98 years, $p=0.021$) and were more likely to be female (97% vs. 79%, $p=0.0001$). They were more likely to report a history of abuse (24% vs. 7% and a family history of an eating disorder (41% vs. 5%, $p=0.002$), and less likely to have a comorbid depression (47% vs. 66%, $p=0.055$).

Management included regular medical monitoring for 166 (91%) of the children and adolescents. Forty cases (22%) received inpatient care, and patients were admitted mostly for medical stabilization or for symptom interruption. Forty children and adolescents (22%) received day hospital treatment. Of note, 14/80 cases received both inpatient and day hospital treatment. The most common mental health intervention was individual therapy in 116 cases (64%), followed by psycho-education in 100 cases (55%) and family therapy in 92 cases (51%). Only 54 cases (30%) were noted to have received

a psychotropic medication, most commonly an antidepressant.

Discussion/conclusion

Little data exists documenting the incidence, presentation, medical complications and treatment of BED symptoms and behaviours in this population in the literature. The intention of this study is to generate hypotheses and, as such, is exploratory in nature. It 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. The high proportion of patients with a medical consequence and psychiatric comorbidity requires further study. These early results confirm the importance of collecting national epidemiological data over several years to ensure that an adequate sample size is obtained, allowing for meaningful interpretations of patterns of presentation and treatment and for a clearer understanding of comorbid medical symptoms and mental health disorders.

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Congenital myotonic dystrophy

March 2005 to February 2010 – Final report

Highlights

- Five years of CMD surveillance confirmed 38 cases for an incidence of 2.1/100,000 live births.
- Of the confirmed CMD cases, 23 (61%) were index cases for their families.
- Withdrawal of life support at one month of age in those children with CMD requiring ongoing assisted ventilation remains a common practice.

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 surveillance study gathered information about the incidence of CMD and the number of children that are index cases for their families. Data were 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 16

CMD cases from March 1, 2005 to February 28, 2010

Year	Reported	Duplicates	Excluded	Pending or unknown	Confirmed
2005*	25	2	3 (16)	0	4
2006	30	12	4 (3)	1	10
2007	24	9	1 (6)	0	8
2008	9	3	1 (1)	0	4
2009	31	14	1 (3)	1	12
2010†	2	0	0 (2)	0	0
Total	121	40	10 (31)‡	2	38

* March 1 to December 31, 2005

† January 1 to February 28, 2010

‡ CMD – not meeting all criteria

Throughout the five years of surveillance, 121 cases were reported. Of these, 38 were confirmed as incident cases. Ten cases were excluded for not meeting the inclusion criteria. Another 31 cases of myotonic dystrophy in children were reported but did not meet all the inclusion criteria. Of these cases, 27 were diagnosed after the age of three or outside of the reporting period, three were not hospitalized for greater than 72 hours, and one was a pregnancy termination. Table 16 demonstrates that one-third of the reported cases were duplicates. The reporting rate for completion of the detailed questionnaire is 95%. Two cases are still of unresolved (pending or unknown) status despite repeated attempts to clarify via the reporting physician.

The estimated minimum incidence of CMD in Canada is 2.1/100,000 live births. This is based on Statistics Canada data for the rate of live births over the surveillance period of calendar year 2005 to year-end 2009. Although some cases were born prior to the start of 2005, we assume that there were also cases born in the later part of our surveillance program that will not come to clinical attention until after the study is completed, thus offsetting the case presentation. If we assume that this is approximately equal cases, then this is an acceptable timeframe to use as the population denominator.

The cases were reported from nine different provinces and one territory. To validate cases, we contacted regional genetic laboratories across Canada to determine, anonymously, how many genetic tests for myotonic dystrophy had been done each year in children less than three years of age. This number was cross-referenced against the provincial reporting to the CPSP (Table 17). Examining the table, one sees that in all cases, except Quebec, the same or more cases of CMD were reported to the CPSP as were tested in provincial labs. There is a possibility of six unreported cases in Quebec.

Of the 38 confirmed cases, 23 (61%) were index cases for their families, 18 were male and 20 were female. The number of CTG repeats was known for 29 confirmed cases with a mean of 1,355 repeats (range 550–3,100). Neonatal mortality

was high with seven children (18%) dying due to complications of CMD. Four of these children died when life support was withdrawn: three at day 27 and one at day 24. Three other children died: two on day one secondary to respiratory failure and sepsis and one child at day 186 due to shock.

TABLE 17

Comparison of CMD confirmed cases: total number, CPSP confirmed and laboratory validated, 2005–2009

Province	Total CPSP confirmed cases	Validated cases by year available	
		CPSP confirmed	Laboratory tested
Ontario	15	15 (2005–2009)	10 (2005–2009, 2007 n/a)
Quebec	6	6 (2005–2009)	12 (2005–2009)
British Columbia	7*	4 (2007 and 2009)	3 (2007 and 2009)
Others	10†	3 (2006 and 2007)	2 (2006 and 2007)

* Three cases - laboratory validation n/a

† Seven cases - laboratory validation n/a

There was great phenotypic variation throughout the confirmed cases, with many children exhibiting more than one neonatal symptom. The most common neonatal complications were feeding and respiratory difficulties. Because of respiratory dysfunction, 27 children (71%) received respiratory therapy. Of those that received respiratory support, 20 (74%) required assisted ventilation for a mean of 25 days (range 1–186). Four of these received prolonged ventilation, lasting more than 30 days. Twenty-nine children (76%) experienced feeding difficulties that led to a nasogastric tube placement with six ultimately requiring a gastrojejunal tube, for a period ranging from two to 176 days. Other complications noted in the neonatal period included ventriculomegaly (n=4), seizures (n=1), club feet or more extensive arthrogyriposis (n=6), and patent ductus arteriosus and other structural heart anomalies (n=5).

All confirmed cases were invited to enrol in a cohort study collecting clinical information and quality of life data over a five-year period. Phone interviews, questionnaires and reports from the primary physician are used for follow-up data. Of the 38 confirmed cases, 17 children have chosen to enrol in the cohort study. Two children have completed the five-year surveillance period.

Conclusion

The CMD surveillance has confirmed 38 cases for an incidence of 2.1/100,000 live births. Of note, 61% were index cases for their families. Surveillance of CMD has been important in order to better document the impact of this disease that 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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Langerhans cell histiocytosis

July 2009 to June 2012

Highlights 2010

- In the first 18 months of surveillance, 17 cases of LCH were confirmed, with 10 this year.
- Mean duration from first symptoms to diagnosis was 13 weeks, with patients often seeing multiple practitioners before diagnosis.

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 18

LCH cases in 2010

Reported	Duplicates	Excluded	Pending	Confirmed
20	5	0	5	10

In 2010, 20 cases of LCH were reported. Of these, 10 were confirmed. Five reports were duplicates of three cases, with one reported by three separate physicians. An additional two cases have been reported by the alternative study pathway: whether these are new or duplicates of previously reported cases is currently unknown.

Of the confirmed cases, there were equal numbers of males and females. The ethnicity of these cases was mainly Caucasian and also included Native American, Inuit, Middle Eastern and Filipino. The mean age at presentation was four years three months (range birth to 16 years). Presenting features were varied. There were five cases of single site bony disease: skull lesions (n=2) and peripheral bone lesions (n=3); and three cases of multifocal bone disease: one each of liver involvement, skin involvement and generalised oedema with gastroenterological disease. Six cases presented first to family practitioners and were referred to the following further specialists before being referred to paediatric haematology/oncology: dermatology (n=1), neurosurgery (n=1), gastroenterology (n=1) and orthopaedics (n=1). The mean duration of symptoms to diagnosis was 16.7 weeks (range 4–56 weeks). Treatment was by observation alone in three cases of single site bony disease and the case of skin involvement. Surgical curettage, followed by chemotherapy (steroids and vinblastine; or steroids, vinblastine, and 6-mercaptopurine), was given in all other cases. One case had been enrolled in the worldwide LCH-III trial.

An additional two outstanding cases were confirmed for 2009, one of which was reported

by the alternate pathway (further details are awaited). Both cases were male with bony disease. One was being treated by curettage only and the other was receiving vinblastine and steroid. The number of confirmed cases for the first 18 months of this study is now 17, with a mean age of three years 11 months and a mean delay time of 13 weeks until diagnosis.

Conclusion

Case accrual is continuing steadily, with some outstanding reports remaining. The case accrual from the alternative study has been slower, although efforts are continuing to obtain further cases.

Most cases involve bony disease. Only one case of skin involvement has been reported to date. Time to diagnosis appears to have lengthened, due in part to two cases with very extended illnesses. Most cases appear to be following a referral route from family physician to paediatrician to paediatric haematologist/oncologist although other specialities are also involved.

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Methicillin-resistant *Staphylococcus aureus* in hospitalized children

September 2008 to August 2010 – Final report

Highlights

- The study confirmed 171 cases of hospitalized children with MRSA infections
- Of confirmed cases, 85% were community acquired and 75% involved skin and soft tissue infections.
- Median length of hospital stay with community-acquired infection was seven days.

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 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 only five provinces and one territory.

Objectives

- 1) Determine the annual number of children requiring hospitalization due to newly diagnosed MRSA infections across Canada
- 2) Describe the clinical spectrum of 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 19

CMRSA cases in hospitalized children from September 1, 2008 to August 31, 2010

Year	Reported	Duplicates	Excluded	Pending	Confirmed
2008*	66	2	19	9	36
2009	131	7	17	23	84
2010†	65	1	7	6	51
Total	262	10	43	38	171

* September 1 to December 31, 2008

† January 1 to August 31, 2010

During the two-year study period, a total of 171 cases of hospitalized MRSA infections were reported from 63 health care centres located in the 10 Canadian provinces and the Northwest Territories. Of these, 60% (102/171) occurred during the second year (September 2009 to August 2010) of surveillance. Physicians determined community acquisition of MRSA in 85% (140/165)¹ of cases with the remainder being hospital acquired.

1. Information was not available on seven cases. Throughout the report, the denominator changes values because of missing information, thus the denominator represents the number of cases with available data.

With 56% (96/171) representation, male patients had a mean age of five years compared to four years for the female patients. Overall, 71% (121/171) of children had no prior underlying medical conditions.

Central (Quebec and Ontario) and far Western (Alberta and British Columbia) Canada reported the highest proportions of cases (Table 20). Urban areas appeared to be the most affected with 73% (122/168) of the cases. Overall, 31% (52/167) of the cases occurred during the months of December to February, 23% (38/167) during March to May, 21% (35/167) during June to August and 25% (42/167) during September to November.

TABLE 20
Reporting provinces or territories

Province/Territory	Frequency (%)
British Columbia	22 (13%)
Alberta	33 (19%)
Saskatchewan	10 (6%)
Manitoba	14 (8%)
Ontario	31 (18%)
Quebec	47 (28%)
Nova Scotia	8 (5%)
Others	6 (4%)
Total	171 (100%)*

* Percentages may not add exactly to 100 due to rounding.

In this study, 17% (28/170) had a known household member infected with MRSA. Available information revealed that 6% (8/129) of the MRSA patients were from two-person households, and 74% (95/129) from three- to five-person households.

The most significant clinical presentations among confirmed cases (Table 21) were skin and soft tissue infections (75%), respiratory infections (15%), and cervical adenitis or abscesses (14%). Bacteremia was reported in 15 patients (9%).

Of the 167 patients for whom admission isolation status was reported, 66% (110/167) were put in contact isolation upon admission whereas 32% (54/167) were isolated only after the MRSA was identified.

TABLE 21
Clinical presentations in MRSA hospitalized paediatric cases (n=171)

Clinical presentations	Frequency (%)
Skin & soft tissue infections*	129 (75%)
Pneumonia (including empyema)	26 (15%)
Cervical adenitis/abscess	23 (14%)
Bacteremia (alone or in combination with other conditions)	15 (9%)
Osteomyelitis	14 (8%)
Septic arthritis	8 (5%)
Fasciitis/Muscle infection	4 (2%)
Ear infection	4 (2%)
Meningitis	3 (2%)
Conjunctivitis	3 (2%)
Mastoiditis	2 (1%)
Other†	10 (6%)

* Cellulitis, boils, infected eczema and abscess that were not cervical

† Umbilical cellulitis, sinusitis, wound infection, toxic shock syndrome, urinary tract infection, dacryocystitis, and dermal sinus tract infection

The mean and median length of hospital stay in 165 cases was 17 and seven days respectively (range 1–197 days). Twenty-nine (17%) children required care in the intensive care unit (ICU) with a mean and median length of stay of 30 days and nine days respectively (range 1–197 days). Of the 157 patients for whom outcome information was available, 150 (95%) were recovering at the time of discharge and seven (5%) were transferred to a rehabilitation facility.

Antimicrobials most frequently used prior to confirmation of MRSA diagnosis, either as single therapy or in combination with other drugs, included cephalosporins (40%), vancomycin (24%), clindamycin (13%) and cloxacillin (10%). Debridement or drainage surgery was performed in 44% (75/171) of the patients (Table 22).

Susceptibilities of MRSA to antimicrobials as reported on the patient charts revealed that 95% (143/150) of isolates were susceptible to trimethoprim-sulfamethoxazole, 65% (98/151) to clindamycin, 46% (16/35) to ciprofloxacin, and 85% (28/33) to doxycycline. Only 3% (4/142) of the isolates exhibited resistance to both trimethoprim-sulfamethoxazole and clindamycin.

TABLE 22**Antimicrobials used on hospitalized paediatric cases of MRSA infections (n= 171)**

Antimicrobial used	Single therapy	Component of the therapy	Overall usage %
	Frequency (%)	Frequency (%)	
Cephalosporin	26 (15%)	43 (25%)	41%*
Vancomycin	10 (6%)	32 (19%)	25%
Clindamycin	6 (4%)	16 (9%)	13%
Cloxacillin	2 (1%)	15 (9%)	10%
Trimethoprim-sulfamethoxazole	3 (2%)	9 (5%)	7%
Clarithromycin and/or azithromycin	0 (0%)	7 (4%)	4%
Ciprofloxacin	5 (3%)	0 (0%)	3%

* Percentages may not add exactly to 41 due to rounding.

Conclusion

Hospitalizations due to MRSA infections in children are occurring in most parts of Canada and, as expected, these infections are primarily community associated. Most of the children are young, with a mean age of five years.

A minority of children were treated initially with vancomycin, indicating either low index of suspicion for MRSA or clinical situations that were not severe enough to warrant initial vancomycin therapy. Most isolates are susceptible to trimethoprim-sulfamethoxazole and clindamycin, making these acceptable alternatives at present. Doxycycline, which also exhibited higher susceptibility, though on a relatively small sample size, could be considered an acceptable first-line option for non-severe MRSA paediatric cases; however, it is contraindicated in children less than eight years of age.

Since the cases are reported primarily by paediatricians, the results may not be representative of hospitalized children with MRSA that are cared for by physicians other than paediatricians, or from rural or more northern areas where fewer paediatricians practise; however, the national scope of the reporting does permit some conclusions.

Further research could focus on risk factors and prognosis for MRSA infections in children.

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Paediatric myasthenia

January 2010 to December 2011

Highlights 2010

- In the first year of surveillance, 33 cases of PM were confirmed.
- A high index of suspicion is required to diagnose PMG; almost half of patients have normal titres of acetylcholine receptor antibodies.
- There appears to be a significant overlap with other autoimmune disorders, particularly thyroid diseases.
- PMG is a treatable disease with readily available treatments, including pyridostigmine, prednisone and intravenous immunoglobulin (IVIG).
- Early recognition and management of PM helps to avoid unnecessary testing, prevents the progression of symptoms and lessens morbidity and mortality.

Background

Paediatric myasthenia (PM) can be divided into two broad categories:

- 1) Paediatric myasthenia gravis (PMG): This is an acquired **autoimmune** mediated disorder causing muscle weakness secondary to antibodies that bind to acetylcholine or other receptors on postsynaptic muscle membranes, so that nerve impulses do not get through to the muscle.
- 2) Congenital myasthenic syndromes: Rare **inherited** conditions caused by structural defects in the neuromuscular junction.

The main features of PM include ptosis, diplopia and extra-ocular muscle weakness (ocular presentation). Many children additionally experience generalized symptoms including rapid fatigue, muscle weakness (worst with repetitive activities), dysphagia, poor head control and respiratory difficulties.

As there are effective treatments and often curative measures for PMG, such as cholinesterase inhibitors, corticosteroids, intravenous immunoglobulin or thymectomy, early detection and diagnosis are in the child's best interest.

It is anticipated that this two-year study will better document the burden of illness and inform on best practices.

Objectives

- 1) Increase awareness of paediatric myasthenia amongst paediatricians
- 2) Reinforce knowledge of myasthenia diagnosis and management

- 3) Ascertain the incidence of paediatric myasthenia
- 4) Determine current treatments offered to myasthenic children across Canada, while observing geographical trends

Case definition

Report any child less than 18 years of age with at least one of the following clinical features:

- Fluctuating ptosis (unilateral or bilateral) and/or
- Fluctuating extraocular muscle weakness (unilateral or bilateral) and/or
- History of skeletal muscle weakness or fatigue

AND any of the following supportive tests:

- Tensilon™ test (edrophonium) (or other acetylcholinesterase inhibitor) demonstrating reversal of weakness
- Elevated acetylcholine receptor or MuSK (muscle specific kinase) antibody levels
- Abnormal nerve conduction studies (demonstrating defect in neuromuscular junction transmission) or single fiber EMG

Exclusion criteria

- Underlying primary muscle disease
- Underlying metabolic disease
- Transient neonatal myasthenia

Results

TABLE 23

PM cases in 2010

Reported	Duplicate	Excluded	Pending	Confirmed
34	0	0	1	33

Overview

In the first year of surveillance, 33 confirmed cases of PM were reported from Ontario, Alberta, Manitoba, Quebec and Newfoundland. There were 19 generalized and 10 purely ocular reports of PMG in children. There were 12 incident cases in 2010: generalized (n=8) and ocular (n=4). Overall, the median age of onset was nine years (range birth to 17 years) for the generalized form compared to four years (range 22 months to 11 years) for the ocular subtype. The ratio of male to female was 10:9 in the generalized group and 3:7 in the younger ocular group. Positive acetylcholine receptor titres were found in 10/18 (56%) of generalized cases and 6/10 (60%) ocular patients. A high index of suspicion is therefore required to diagnose PMG; almost half of patients did not have elevated screening acetylcholine receptor antibodies. In these cases, further precise diagnostic evaluation was required. There were four reports of congenital myasthenic syndrome.

Initial treatments

For patients presenting with generalized symptoms, early treatment course information was available for 18 patients. All were started on pyridostigmine; improvement was noted in 17/18 (94%). Ten patients received steroids; improvement was cited in 9/10 (90%); it was too early to evaluate the effect in the remaining patient. Eleven patients were tried on IVIG; there was reported improvement in 9/11 (82%).

For patients with exclusively ocular presentations, all 10 were started on pyridostigmine. Improvement occurred in 8/10 (80%). One patient did not improve and the outcome was not indicated in the other case. Six patients were started on prednisone. Results were available in five cases; all improved. One patient, who was acetylcholine receptor

antibody positive, was treated with just one course of IVIG, without appreciable effect.

Associated conditions

There was an apparent high association of PMG with thyroid disorders. Two antibody positive patients were concurrently diagnosed with Grave's disease. In an additional three cases, there was a family history of Hashimoto's or other autoimmune thyroid disease. Furthermore, the mothers of two patients were diagnosed with multiple sclerosis.

Conclusion

This ongoing study, which represents the largest descriptive series of paediatric myasthenia in North America, provides valuable information about clinical characteristics and raises awareness regarding the diagnosis. A high index of suspicion is required even in patients with normal titres of acetylcholine receptor antibodies. PMG is a treatable disease. Children generally respond promptly to readily available treatments including pyridostigmine, prednisone and IVIG. Early recognition and management of PM helps to avoid unnecessary testing, prevents the progression of symptoms, and lessens morbidity and mortality.

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Persistent albuminuria in the paediatric population with type 2 diabetes mellitus

April 2010 to March 2012

Highlights 2010

- After nine months of surveillance, 14 cases of persistent albuminuria have been confirmed in children less than 18 years of age with type 2 diabetes mellitus.
- Preliminary results indicate that children of Aboriginal heritage appear to be disproportionately affected.
- Ongoing data collection is important to confirm trends and gather data regarding the clinical characteristics of the affected population. This information may help inform future prevention and/or treatment strategies.

Background

The prevalence of childhood-onset type 2 diabetes mellitus (T2DM) is increasing. A recent CPSP study revealed a minimum incidence of T2DM in children less than 18 years of age in Canada of 1.55 cases per 100,000 children per year with a sensitivity analysis suggesting a maximum incidence of 40.5 cases per 100,000 children per year. Significant regional variation has been identified with the highest rates of T2DM observed in Manitoba.

In adults, end-stage complications of T2DM occur within 20 years. The natural history of T2DM diagnosed in childhood is still largely unknown. The first sign of diabetic nephropathy is persistent microalbuminuria, which may progress to macroalbuminuria and ultimately end-stage renal failure (ESRF) requiring renal replacement therapy. Evidence suggests that complications occur at an earlier age with a shorter duration of diabetes in youth-onset T2DM.

The earlier age of diagnosis raises concern regarding the resulting burden of disease as these children may begin to develop complications of diabetes as young adults at the height of their productivity and child bearing years, resulting in significant impact on quality of life as well as economic consequences.

Objectives

- 1) Determine the minimum prevalence of persistent microalbuminuria and macroalbuminuria in children <18 years of age in Canada with T2DM
- 2) Characterize the clinical features at diagnosis of diabetes associated with persistent

microalbuminuria or macroalbuminuria in children <18 years of age in Canada with T2DM

- 3) Identify the clinical features that can help distinguish diabetic and non-diabetic renal disease in children <18 years of age in Canada with T2DM

Case definition

Report any patient up to 18 years of age with type 2 diabetes mellitus

and

persistent microalbuminuria or macroalbuminuria, defined as 2/3 positive samples at least one month apart over a 3–6 month period.

Canadian Diabetes Association definition of diabetes:

- Fasting plasma glucose (FPG) ≥ 7.0 mmol/L* or
- Random plasma glucose ≥ 11.1 mmol/L* or
- Two-hour plasma glucose ≥ 11.1 mmol/L* after a standard oral glucose tolerance test

* Requires a second, confirmatory test if child is asymptomatic

Diagnosis of T2DM will be based on the following clinical features:

- Obesity (body mass index $>95^{\text{th}}$ percentile for age and gender)
- Family history of T2DM in a first or second degree relative(s)
- Belonging to a high-risk ethnic group (e.g., Aboriginal, African, Hispanic, South-Asian)
- A history of exposure to diabetes in utero (diagnosed before or during pregnancy)

- Evidence of insulin resistance: acanthosis nigricans, polycystic ovarian syndrome, hypertension, dyslipidemia
- Absence of diabetes-associated autoantibodies when available

TABLE 24

Definition of albuminuria*

	Urine albumin to creatinine ratio (ACR) [†]	24-hour urine collection for albumin
Microalbuminuria	2.0–20.0 mg/mmol (male) 2.8–28.0 mg/mmol (female)	30–300mg/day (male or female)
Macroalbuminuria	>20.0 mg/mmol (male) >28.0 mg/mmol (female)	>300 mg/day (male or female)

* Persistent albuminuria defined as 2/3 positive samples over a 3–6 month period, samples must be at least one month apart

† Confirmation with either first-morning urine sample or overnight urine collection

Results

TABLE 25

Persistent albuminuria in youth with type 2 diabetes mellitus cases from April 1 to December 31, 2010

Reported	Duplicate	Excluded	Pending	Confirmed
17	0	0	3	14

During the first nine months of surveillance, 17 cases of persistent albuminuria in youth with type 2 diabetes have been reported. Of these, 14 are confirmed and three are under review. There have been no duplicate reports.

Of the 14 confirmed cases, 10 (71%) are female and all were of self-declared Aboriginal heritage (13 First Nations, one Métis). The mean age at diagnosis of albuminuria was 13.6 years \pm 1.68 (range 10.0 to 16.8 years) (male 12.9; female 13.9 years). Associated co-morbidities were common, with hypertension the most frequently reported in 8/14 cases (57%), dyslipidemia in 6/14 (43%) and non-alcoholic liver disease in 6/14 (43%).

Conclusion

Preliminary results indicate that persistent non-orthostatic albuminuria in youth with type 2 diabetes does occur in Canada and that children of Aboriginal heritage appear to be disproportionately affected. National surveillance for the prevalence of albuminuria in children with T2DM is necessary to define the spectrum and extent of the problem. This is important for predicting burden of illness and for planning screening and intervention programs. This data will be useful for paediatricians, community physicians, community health professionals, policy makers and program planners. Furthermore, this will provide a baseline prevalence estimate for future comparison. Identification of the population of children affected with T2DM and albuminuria will facilitate research to understand the etiology and prevention of this significant complication.

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Respiratory syncytial virus (RSV) infections in paediatric transplant patients

September 2010 to August 2013

Highlights 2010

- The incidence of RSV infections in paediatric solid organ or hematopoietic stem cell transplants is unknown.
- There is no published data on use of palivizumab in transplant recipients.

Background

Children with prematurity, chronic lung disease (CLD) or immunodeficiency have markedly higher risks of hospitalization and intensive care stays with respiratory syncytial virus (RSV) infection. The magnitude of this increased risk has not been quantified in solid organ transplant (SOT) (liver, heart, lungs, kidneys, intestines) or hematopoietic stem cell transplant (HSCT) recipients.

Quantifying the true risk of severe RSV infection for different types of transplants and different age groups at various times post-transplant has become of practical importance as the monoclonal antibody palivizumab is now used as RSV prophylaxis in some transplant recipients. Serious adverse events are very rare with palivizumab and it prevents about half of RSV hospitalizations in children with congenital heart disease or CLD related to prematurity, and about 80% in children with prematurity and no CLD. However, palivizumab has not been formally studied in transplant recipients, requires one or more monthly injections throughout RSV season, and is very expensive.

Objectives

- 1) Estimate the incidence of RSV infections requiring hospitalization within two years following SOT or HSCT
- 2) Determine if the type of transplant alters the risk of hospitalization with RSV
- 3) Describe the length of stay and need for intensive care for transplant patients admitted with RSV, and determine if the type of

transplant or time since transplantation alters these factors

- 4) Determine if children with infections from RSV within two years of a transplant are ever successfully managed as outpatients

Case definition

Report all inpatients and outpatients less than 18 years of age who have:

- Laboratory-confirmed RSV infection
- and**
- Received solid organ transplantation or haematopoietic stem cell transplantation within the two previous years.

Results/discussion

In Canada, the RSV season typically starts in November or later. Therefore, it is not surprising that only one case was reported in the first four months of surveillance. As RSV prophylaxis is available, gathering data on the incidence and the morbidity associated with RSV infection in Canadian transplant recipients is of utmost importance to establish potential costs and benefits of palivizumab. As many patients receive their ongoing care outside of transplant centres, the study will also seek to determine if physicians ever manage known RSV infections in transplant recipients on an outpatient basis.

Conclusion

This study will be the first to collect data on the incidence of RSV infection up to two years after SOT or HSCT. It is imperative that the small number of anticipated cases all be reported.

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Serious adverse events associated with paediatric complementary and alternative medicine

January 2009 to December 2010 – Final report

Highlights

- Few cases of serious adverse events associated with paediatric complementary and alternative medicine have been reported.
- Adverse events may be “direct,” due to the therapy itself, or “indirect,” due to a delay in diagnosis or treatment.
- In the majority of cases, the family initiated CAM therapy without the advice of a health care professional.
- 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 cases 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 associated with the use of complementary and alternative medicine§.

* 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 26

Serious adverse events associated with paediatric CAM cases from January 1, 2009 to December 31, 2010

Year	Reported	Duplicate	Excluded	Pending	Confirmed
2009	8	1	0	1	6
2010	5	0	1	2	2
Total	13	1	1	3	8

In the two-year study period, 12 unique cases (one case was reported twice by different physicians) of adverse events associated with CAM were reported by paediatricians across Canada (Table 26). Another three cases were reported, but as the detailed questionnaires remain pending they could not be adjudicated. Nine cases were adjudicated by the steering committee of the research team and

eight of those were considered serious. The ninth case did not fulfill the World Health Organization (WHO) criteria for seriousness and was therefore excluded as it did not meet the study inclusion criteria. The WHO criteria for seriousness include any case that: (i) results in death; (ii) is life-threatening; (iii) requires or prolongs hospitalization; (iv) causes persistent disability/incapacity; (v) results in congenital anomalies or birth defects; or (vi) results in any other condition which in the judgment of the adjudicators represents significant hazards.

Of the adjudicated serious cases, six were from Central Canada and the remainder were from Western Canada. Of note, the family initiated the CAM therapy without the advice of a health care professional in the majority of cases. CAM therapies used included: products, such as bee pollen, Chinese herbs, tea made from the datura plant and vitamin D; and practices, such as healing touch pseudo-immunotherapy, blood-type diet, osteopathy, Chinese traditional medicine and spinal manipulation (Table 27).

The reports of adverse events vary from anaphylaxis and hallucinations to muscle weakness with elevated creatine kinase. In addition, a vitamin D overdose was reported with possible chronic nephrocalcinosis as a consequence. One patient had short-

term paralysis, possibly associated with spinal manipulation.

Indirect harms associated with CAM use were also reported, such as treatment delay for a child with juvenile idiopathic arthritis and another with Crohn's disease. Diagnostic delay of anorexia nervosa with significant weight loss associated with a blood-type diet was seen in one patient.

Importantly, this study has contributed to the development of an adjudicating process to assess direct and indirect harms associated with any therapy, not exclusive to CAM, whether it is a product, practice or device. The interpretation of data results was based on both the cases and the adjudicating algorithm that was developed to support case assessment.

Conclusion

Very few AEs were identified in this study, despite widespread use of paediatric CAM. While surveillance studies always carry the risk of under-reporting, study data suggest that serious harms are rarely reported with paediatric CAM use. Safety assessments benefit from consideration of both direct (product, device or practice) and indirect (delay in diagnosis and/or treatment) harms. Clinicians are encouraged to ask about CAM use at every patient visit and report any suspected serious events to the CPSP study on adverse drug reactions (p. 22).

TABLE 27

Summary of cases, CAM, adverse events and adjudication results

Confirmed suspected case	CAM	Adverse events (AE)	Classification of AE		Adjudication
			Direct	Indirect	
Juvenile idiopathic arthritis	'Healing Touch' pseudo-immunotherapy	Progression of juvenile idiopathic arthritis		Treatment delay	Probable
Allergic rhinitis	Bee pollen	Anaphylaxis	Product		Probable
Upper respiratory tract infection	Chinese herbs	Rhabdomyolysis	Product		Possible
Constipation	Blood-type diet	Weight loss	Practice	Diagnosis delay Treatment delay	Direct: probable Indirect: probable
Chronic psoriasis	Datura tea	Hallucinations	Product		Probable
Bloody diarrhea	Osteopathy/ traditional Chinese medicine	Anaemia and progression of Crohn's disease		Diagnosis delay Treatment delay	Probable
Healthy child	Vitamin D supplementation	Vomiting, hypercalcemia, hypertension	Product		Probable
Back pain	Spinal manipulation	Spinal cord ischemia	Practice		Possible

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Publications and presentations

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Severe combined immunodeficiency

April 2004 to March 2010 – Final report

Highlights

- From April 2004 to March 2010, 44 cases of SCID were confirmed, representing an estimated incidence of two cases per 100,000 births.
- Aboriginal children were over-represented, accounting for 16% of the confirmed cases.
- The average age at diagnosis was four months. Earlier diagnosis carries a better prognosis, as hematopoietic stem cell transplantation can be performed before the appearance of severe infections.

Background

Severe combined immunodeficiency (SCID) is a life-threatening condition with high morbidity and mortality. As part of the strategy to reduce the incidence and severity of tuberculosis (TB), the First Nations and Inuit Health Branch (FNIHB) of Health Canada has recommended the use of the Bacille Calmette-Guerin (BCG) vaccine for newborns. Infants who have SCID and who are immunized with this live bacterial vaccine are at high risk of severe complications of disseminated BCG infection, a severe complication of the vaccine in certain immunocompromised persons. 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, four of which were infants with undiagnosed SCID. This CPSP project aimed to determine the incidence of SCID in Canadian infants, focusing on Aboriginal children.

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 human immunodeficiency virus (HIV) infection or cystic fibrosis.

Results

TABLE 28

SCID cases reported from April 1, 2004 to March 31, 2010

Year	Reported	Duplicates	Excluded	Pending	Confirmed
2004*	22	13	3	0	6
2005	19	9	1	0	9
2006	15	6	2	0	7
2007	22	11	1	0	10
2008	9	5	0	0	4
2009	15	6	1	0	8
2010†	0	0	0	0	0
Total	102	50	8	0	44

* April 1 to December 31, 2004

† January 1 to March 31, 2010

Detailed questionnaires were not received for all reported cases, but extensive follow-up by the investigators allowed for 100% of reported cases to be included or excluded from the study. During the six years of surveillance, Canadian paediatricians and paediatric subspecialists reported 102 suspected cases of SCID to the CPSP. Of these, 50 forms were duplicates and eight had to be excluded according to the case definition of the study. No excluded cases had HIV infection or cystic fibrosis.

SCID was confirmed in 44 cases, representing an estimated incidence of two cases per 100,000 births, basing the birth denominator on data from Statistics Canada. The average age at diagnosis was four months (range 0–15 months). There were twice as many males as females (30 versus 14 cases). All but one of the confirmed cases were born in Canada: six were First Nations infants and one was an Inuit infant. Cases were from different provinces/territories, with most cases diagnosed in Ontario and Quebec.

Since numbers of births are not available for the Aboriginal population, it was not possible to calculate an incidence rate for this population. Nonetheless, Aboriginal children accounted for 16% of the confirmed cases, but comprise 4% of the total Canadian population (according to Statistics Canada 2006 census).

The main clinical features documented were interstitial pneumonia, failure to thrive, persistent bronchiolitic-like illness and other significant infections (e.g., *E. coli*, influenza, respiratory syncytial virus). Several rare genetic diseases were identified, the most common of which was X-linked SCID (nine cases), ADA-deficient SCID (nine cases) and RAG-deficient SCID (five cases). SCID types were not specified for 10 cases. Almost half of the cases (21) had a family history of immunodeficiency (sibling with immunodeficiency) or suggestive of immunodeficiency (infant death from infections, parent's consanguinity). Only the child born outside Canada was reported as being immunized with the BCG vaccine (information was not available for three cases).

Ten children died before they could receive a hematopoietic stem cell transplantation (HSCT) either while they were waiting to receive it, because they were not a candidate (e.g., too sick to receive an HSCT) or parents chose a palliative approach. Twenty children were reported to have received HSCT, of which four died post transplantation. Information on treatment was missing for four cases.

Conclusion

This national prospective active SCID surveillance study identified 44 cases of SCID for an overall estimated incidence of two cases per 100,000 births.

Aboriginal infants accounted for 16% of SCID cases but account for 4% of the total Canadian population. This finding suggests that Aboriginal infants are over-represented, in keeping with other studies on the incidence of SCID in Aboriginal populations in the United States. Several genetic diseases were responsible for SCID cases. Accordingly, FNIHB plans to continue gradual BCG discontinuation, where the epidemiology and local parameters support this, replacing vaccination with enhanced preschool TB screening as a strategy to control tuberculosis.

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Publications and presentations

Fontaine J, Ramsingh R, Junker A, Yacoub W, Long R, Langley JM, Embree J, Schultz K, Grenier D. Severe combined immunodeficiency syndrome in the Aboriginal population in Canada – Implications for BCG vaccination. 15th Annual Conference of the International Union against Tuberculosis and Lung Disease – North America Region, Vancouver, February 2011. (Poster presentation)

Rozmus J, Fontaine J, Junker A, Embree J, Langley JM, Schultz K, Ramsingh R. Surveillance for severe combined immune deficiency (SCID) syndromes in Canada. Primary Immune Deficiency Treatment Consortium (PIDTC) Scientific Workshop, San Francisco, April 2011. (Poster presentation)

Severe iron-deficiency anemia in infants and young children

October 2009 to September 2011

Highlights 2010

- Severe iron-deficiency anemia continues to occur in Canada, with 71 confirmed cases in 2010.
- The mean age at presentation was 18 months.
- In confirmed cases, dietary factors such as excessive milk and/or inadequate meat intake were involved.
- Over half (54%) of the cases were admitted to hospital and 23% had complications, such as developmental delay and congestive heart failure.

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 breast-feeding 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 29

Severe IDA cases in 2010

Reported	Duplicates	Excluded	Pending	Confirmed
146	5	19	51	71

In 2010, 146 cases of severe iron-deficiency anemia were reported in infants and young children. Nineteen cases were excluded for the following reasons: not meeting inclusion criteria for anemia (n=5), age (n=6), confirmatory biochemical laboratory test such as ferritin (n=3), recorded blood test results (n=1), inability to locate chart/patient by respondent (n=3), presence of a disease known to be associated with anemia (n=2) and child excluded by physician (n=1). Seventy-one cases were confirmed. The mean age was 18 months (range 7–35 months). Over half of the cases were Caucasian (n=37/67, 54%), 23 (34%) were Asian, three (5%) each were Aboriginal and mixed, and two (3%) were Middle Eastern. This suggests an over-representation of the Asian population, as they represent 11% of the Canadian population (Statistics Canada, 2006 Census). The Aboriginal population might be under-represented, as very few paediatricians are working in remote northern communities.

The mean hemoglobin level was 57 g/L (range 13–79 g/L), mean MCV was 53.2 fL (range 39.5–70 fL), and mean serum ferritin was 7.2 µg/L (range <1–46 µg/L, excluding one patient with a ferritin of 144 µg/L in the context of an acute infectious illness and good response to oral iron therapy).

Of the 59 infants receiving cow's milk at the time of the report, the mean daily consumption was 1.1 L (38 oz), range 200 mL to 2.4 L (7–81 oz), and 32 were reported to have inadequate meat intake. Forty-seven (66%) infants were currently or previously breast-fed. Presenting signs that prompted the physician to request laboratory investigations included pallor (n=46), developmental delay (n=4), poor energy (n=15), fever (n=14), irritability (n=13), infectious

illness (n=25), edema (n=8), pica (n=3) and poor feeding (n=5). Almost a quarter (23%) had complications, namely evidence of heart failure (n=5) and of developmental delay (n=11). In all cases, the attending physician prescribed oral iron supplementation and provided dietary counselling. Over half (54%, n=38) were admitted to hospital, seven children required a blood transfusion and 12 had a consultation with a paediatric hematologist. Transfusions for children with IDA are usually limited to cases of severe anemia with complications. The mean reported hemoglobin level in children requiring a blood transfusion in the study population was 37 g/L (range 13–76 g/L).

Conclusion

The results from these 12 months of surveillance demonstrate that severe IDA is being reported in Canadian infants and young children and is associated with significant morbidity. Dietary factors were involved in most confirmed cases, including high consumption of cow's milk and inadequate meat intake. Primary prevention through nutrition counselling of young children may lead to reductions in severe IDA. Secondary prevention through screening young children, especially those with high risk factors, for early stages of iron deficiency before the onset of anemia should be an area for future research.

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

March 2009 to February 2011

Highlights 2010

- In 2010, 44 confirmed cases of significant travel-related illnesses occurred among paediatric travellers who visited friends and relatives abroad.
- Enteric fever (“typhoid fever”) and malaria were the most common types of travel-related illnesses.
- A majority of confirmed cases did not obtain pre-travel advice.
- Almost two-thirds required hospitalization with an average length of stay of 13 days.

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, antimalarial 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 30

TRIP-VFR cases in 2010

Reported	Duplicates	Excluded	Pending	Confirmed
66	2	2	18	44

In 2010, the study confirmed 44 cases of travel-related illnesses in paediatric VFRs (Table 30). Among these, 16 (36%) were reported from Ontario, nine (20%) from Quebec, seven (16%) from British Columbia, five (11%) each from Manitoba and Alberta, and the remaining cases were from Saskatchewan and Prince Edward Island. The regions of travel and the types of TRIs acquired by paediatric VFRs are summarized in Figure 3 and Table 31.

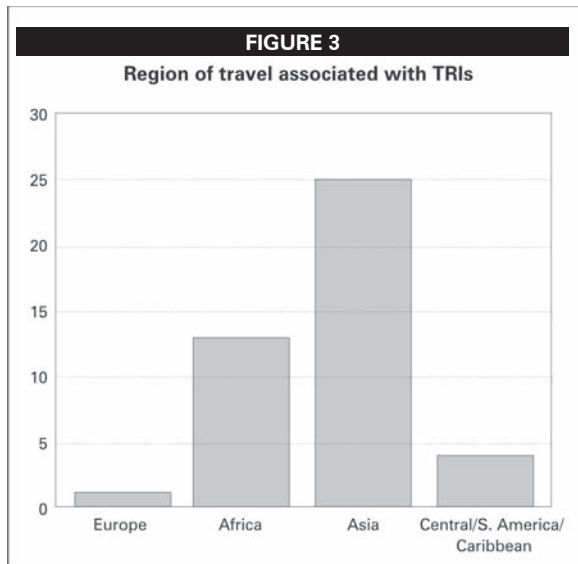


TABLE 31
Types of TRIs acquired by paediatric VFRs

Enteric fever (suspected/confirmed)	16 (1/15)
Malaria	11
Severe diarrheal illness	6
Hepatitis A	3
Parasitic infections	2
Dengue	2
Leishmaniasis	1
Brucellosis	1
Non-typhoidal <i>Salmonella</i> bacteremia	1
TB symptomatic disease	1

The majority (84%) presented with fever. Diarrhea (36%), abdominal pain (16%), vomiting (14%), cough (14%), rash (11%) and headache (11%) were also common symptoms. Almost half (45%) of the malaria cases presented with gastrointestinal or respiratory symptoms, as well as fever. The majority of patients with TRIs were initially seen in the

emergency department (70%) as compared to the office or clinic (30%).

The interval of time between the beginning of travel and the onset of symptoms ranged from a few days to several months with an average of 79 days due to the long duration of travel for some children. 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 seven weeks. Three-quarters of the VFR children travelled to urban areas with 39% exclusively to urban areas and 36% to both rural and urban areas. Only 7% travelled exclusively to rural locations. All confirmed cases, whose type of accommodation was known, stayed in family homes, only 13% 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 (17%), unpasteurized dairy products (10%), and uncooked or unpeeled fruits and vegetables (20%).

Among the 44 confirmed cases, 11 obtained pre-travel advice, 23 did not, and in eight cases it was unknown whether any advice was received. Of those who received pre-travel advice (n=11), two obtained it from a travel clinic physician, two from a paediatrician, one from a family doctor, and six respondents did not specify by whom the advice was provided.

Of those who obtained pre-travel advice, one patient was compliant with the pre-travel advice but still developed severe post-infectious travellers' diarrhea with significant sequelae. Three patients were not compliant with the advice given (refusal of vaccines or antimalarial recommendations). In seven cases it was unknown if the advice was given correctly and not followed or was inappropriate. For example, for two patients who developed enteric fever, it was indicated that they were compliant with their pre-travel vaccine advice, but no vaccines were listed as having been given. Several patients who were prescribed appropriate antimalarials "ran out" or did not take them for a long enough period upon their return.

Three-quarters of patients with TRIs required hospitalization (n=34) with an average length of stay of 13 days (mean=13, median=5). Of note, two patients required admissions of approximately three months duration. Two patients presented with hypotension (malaria) or septic shock (enteric fever). There were no deaths.

Conclusion

In 2010, there were 44 confirmed cases of significant travel-related illnesses among paediatric VFRs as compared to 33 confirmed cases during the first 10 months of surveillance in 2009. These numbers likely under-represent 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 study from both 2009 and 2010 are consistent with information regarding TRIs among adults, given that paediatric VFRs generally travelled for at least several weeks, stayed in family homes, and ingested unsafe food and water. The majority of TRIs occurred in children who travelled to Asia. Only a quarter of the paediatric VFRs sought travel advice, and among those who did, less than 20% obtained advice from a travel medical clinic.

The majority of paediatric VFRs required hospitalization for their TRIs with an average length of stay of 13 days (mean=13, median=5), while two patients required admissions of approximately three months duration. The average length of stay in 2009 was six days, which indicates an increase in the average length of stay of more than 115%. Consequently, there is

significant morbidity among paediatric VFRs in Canada. Furthermore, the majority 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. Travel-related illnesses in Canadian children. Canadian Paediatric Society Annual Conference, Vancouver, June 2010. (Poster presentation)

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



Baby products injury

February 2010

Designed in partnership with the Public Health Agency of Canada, the Consumer Product Safety Bureau (CPSB) at Health Canada (HC) and the Canadian Paediatric Society, the CPSP conducted a one-time survey focused on the frequency and extent of injuries associated with cribs, baby walkers and strollers in Canada.

The response rate was 27% (658 responses of 2,466 participants). Overall there were 92 reported incidents, including some serious injuries as shown in Table 32.

TABLE 32

Reported incidents with strollers, baby walkers and cribs (n=92)

Injuries	Strollers n=58 (63%)	Baby Walkers n=19 (21%)	Cribs n=15 (16%)
Concussions	4 (7%)	1 (5%)	1 (7%)
Skull fractures	1 (2%)	0	3 (20%)
Upper extremity fractures	2 (3%)	0	1 (7%)
Lower extremity fractures	1 (2%)	2 (11%)	1 (7%)
Abrasions/lacerations	16 (27%)	5 (26%)	2 (13%)
Abrasions/lacerations	34 (59%)	11 (58%)	7 (47%)

The CPSP also collected information on the dissemination and knowledge transfer of the bans/ advisories and recalls issued on these products by HC.

In January 2010, a recall notice for certain stroller models was issued, after reports of finger amputations and lacerations were identified in association with specific models and an additional advisory followed reminding Canadians to exercise caution when using strollers with hinge

mechanisms. Awareness of all respondents to these measures was indicated in the survey as follows: approximately 53% were aware of the stroller recall; 43% of the stroller advisory; and 36% knew both. Just over 75% of those respondents who reported how they learned of the recall and/or the advisory indicated it was through news media reports (i.e., newspaper, radio, TV, Internet).

The CPSB investigated reports of serious head injuries associated with falls while in baby walkers which ultimately lead to a ban on baby walkers in Canada. Since April 2004, it is illegal to import, advertise for sale, or sell baby walkers in Canada, including at garage sales, flea markets, or on street corners. The respondents indicated that 83% were aware of the prohibition of baby walkers. Approximately 40% of those respondents who reported how they learnt of the ban indicated it was through the news media.

Over 80% of the paediatricians surveyed reported spending time advising parents/caregivers of infants and young children on safety practices in their home; almost two-thirds provide advice on hazards associated with baby products.

Just over half of respondents indicated that ‘yes’ they required education materials on the selection of safe baby products for their patients; over 80% of these respondents preferred it in the form of a pamphlet/brochure. The majority of respondents (83%) indicated that improved communication of product hazards to the paediatric health professionals was necessary.

The CPSP survey confirmed that serious injuries associated with strollers, baby walkers and cribs are still occurring in Canada; that recall/ advisory notices reached approximately one-half of respondents, while news media seemed more

effective; and that frontline health care providers needed more education materials.

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Complications associated with infant male circumcision

December 2010

A one-time survey was circulated to all 2,508 CPSP participants to assess if they recalled seeing complications arising from infant male circumcisions within the past 12 months only. CPSP participants include paediatricians and paediatric subspecialists but do not include paediatric surgeons or surgical subspecialists or general practitioners performing circumcisions. There were 786 responses (response rate = 31%).

The complications reported were typical of those reported in the literature. The vast majority recalled no specific complications of infant male circumcisions. Others reported minor complications, such as local infection, hematoma, minor bleeding, and cosmetic concerns. Major complications included sepsis, severe bleeding requiring transfusion, amputation and infarction. Some respondents reported a single case, while others reported multiple cases. There were no reports of death, permanent disability or HSV infections. Respondents were also asked to identify which complications led to hospitalization. Many respondents left this column blank, but bleeding and

infection were the predominant complications leading to hospitalization. In some cases, the respondent assumed causation for a complication, for example, sepsis or meningitis secondary to the circumcision.

The survey also asked respondents who identified complications to indicate the technique of circumcision used and the professional category of the individual who performed the procedure. The technique used for the circumcision was rarely recalled on the survey forms. Plastibell, Gomco and Mogen were all reported by at least one respondent. Plastibell and Gomco were the most commonly used instruments. The practitioner type was recalled by slightly over half of respondents: Circumcision was performed almost equally by paediatricians, general practitioners or surgical specialists (including general surgeon, paediatric surgeon, urologist, and gynaecologist) and one non-medical/cultural provider.

A small number of respondents indicated they referred infants to a surgical specialist for complications of circumcision, usually for bleeding issues or corrective procedures.

This survey is a very preliminary snapshot and has many limitations including, but not limited to: low response rate, incomplete respondent recall; lack of specific verification of any report; multiple individuals possibly recalling the same case; lack of a denominator (number of circumcisions performed and under what circumstances); assumed causation; incomplete data submission. The report of potentially serious complications in this preliminary survey would indicate a need for a more formal surveillance system to capture, verify and quantify these rare complications. Once the complications are identified, steps can be put in place to remedy and prevent these occurrences.

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Patients with asymptomatic adrenal suppression

March 2010

Glucocorticoid (GC) therapy is extremely effective for the treatment of several paediatric diseases. Among the potential side effects is adrenal suppression (AS) which results in an inability to produce adequate amounts of cortisol – a critical hormone during physiologic stress. Children with AS may be asymptomatic, have non-specific signs and symptoms (e.g., fatigue, nausea, poor growth) or be critically ill (i.e., adrenal crisis). Adrenal crisis and its associated morbidity and mortality can be prevented by recognizing children at risk for AS and administering adequate doses of GCs during times of stress. Children with asymptomatic AS can only be diagnosed as a result of screening. Official guidelines for AS screening have yet to be developed. Consequently, screening practices are highly variable between physicians and centres.

Before launching a two-year surveillance study to estimate the incidence, clinical features, and burden of illness of symptomatic AS in the Canadian paediatric population, participants were surveyed to assess their screening practices for AS and their recognition of asymptomatic cases. The objectives of the survey were to: (1) collect data on recognized cases of asymptomatic AS and current screening practices to detect these cases, (2) estimate the prevalence of Canadian children being treated with GCs, and (3) measure the educational impact of the surveillance study by comparing results with a subsequent post-study survey. Identifying and treating asymptomatic patients *before* they develop symptoms can lead to reduced morbidity in this population.

The one-time pre-study survey was sent to all 2,548 CPSP participants in March 2010. Eight hundred and twenty paediatricians responded (32% response rate). Eighty-four percent of respondents have seen children/youth treated with GCs within the last month. Of those who reported seeing GC-treated

children, 86 (13%) saw less than 5, 155 (23%) saw 5-10, 198 (30%) saw 11 to 20, 145 (22%) saw 21 to 50, 53 (8%) saw 51-100, and 25 (4%) saw more than 100. Eighty (10%) paediatricians routinely screen patients on GCs for AS. Fifty-one (6%) paediatricians reported having a screening policy for AS in their office/centre.

Ninety-six (12%) paediatricians reported seeing at least one case of asymptomatic AS over the past year. For these children, the underlying condition requiring GC treatment was asthma in 63 cases (50%), inflammatory bowel disease in 20 (16%), malignancy in 23 (18%), nephrotic syndrome in 9 (7%), and a rheumatologic condition in 12 (9%). Diagnosis was made by a first morning cortisol in 71 cases (74%), standard-dose ACTH stimulation test in 30 (31%), low-dose ACTH stimulation test in 20 (21%), random cortisol in 14 (15%), 24-hour urinary cortisol in 4 (4%), and “other” in 13 (14%).

Survey results suggest that many children in Canada are being treated with GCs for various conditions. There is a wide variability in screening practices for AS among physicians and centres. While the low-dose ACTH stimulation test is now considered to be the best test for the diagnosis of AS by most endocrinologists, a first morning (08:00) cortisol level is more practical and frequently used as an alternative. The relative percentage of children being screened for asymptomatic AS is minimal compared with those being treated with GCs. Hopefully, with increased awareness, more children should be diagnosed with and treated for asymptomatic AS. Study results might also inform on the development of clinical practice guidelines for the screening of AS.

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

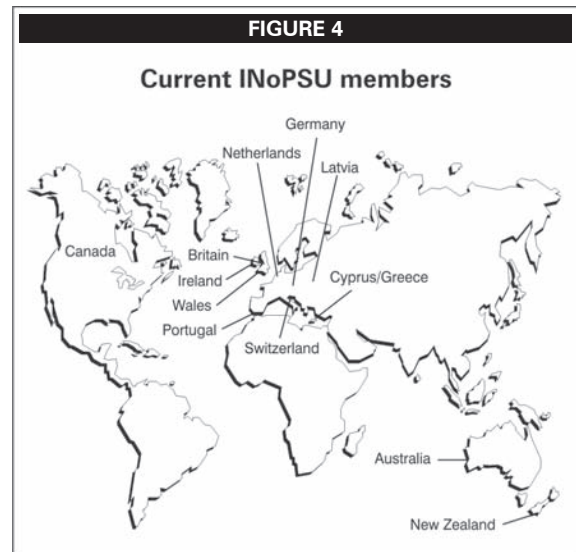
2010 highlights

The 6th INoPSU meeting was held in Dublin, Ireland on October 7–8, 2010, and coincided with the Faculty of Paediatrics of the Royal College of Physicians of Ireland annual scientific conference. Fifteen representatives from seven different INoPSU units were present (www.inopsu.com).

The meeting provided an excellent opportunity for representatives from each of the national units to meet and exchange views on rare disease surveillance and discuss issues that currently pose challenges to the units. Funding and ethical approval of surveillance studies were a particular focus.

The two-day meeting comprised a one-day scientific meeting, followed by the INoPSU business meeting. The scientific program included the following presentations:

- Key note address by Dr. Ségolène Ayme from Orphanet: Improving the medical care in rare diseases



- HIV/AIDS and lead poisoning in children (Ireland)
- Pandemic influenza H1N1 in children (Australia)
- Surveillance and beyond: The Canadian experience; Challenges and responses: The Canadian Paediatric Surveillance Program; and Public health impacts of INoPSU (Canada)
- Sexually-transmitted infections, tuberculosis, toxic shock syndrome, early-onset eating disorders, lead poisoning, and fast-track surveillance for public health emergencies (United Kingdom)

Yvonne Zurynski from Australia and Danielle Grenier from Canada were elected as new INoPSU co-chairs for the next three years.

Preparations are well underway for the 7th INoPSU meeting to be held in Montreux, Switzerland, September 1–2, 2011. The meeting will be hosted by the Swiss Paediatric Society.

Rare Disease Day – February 28 www.rarediseaseday.org

Rare Disease Day is marked across the globe as an annual, awareness-raising event coordinated by EURORDIS at the international level and by the International Alliance of Patients' Organizations at the regional level.

In the United Kingdom, Rare Disease Day is being coordinated by the Genetic Alliance UK, an interest group for all people affected by genetic conditions, and Rare Disease UK, a group brought together to develop strategic planning for rare diseases.

INoPSU units were involved in several activities. The Australian Paediatric Surveillance Unit hosted a workshop on rare diseases at the Children's Hospital at Westmead in Sydney, on February 27, 2010.

Publications from INoPSU members

Australian Paediatric Surveillance Unit (APSU)

He S, Zurynski Y, Elliott E. What do paediatricians think of the Australian Paediatric Surveillance Unit? *J Paediatr Child Health* 2010; 46: 412-8

Jaffe A, Zurynski Y, Beville L, Elliott E. Call for a national plan for rare diseases. *J Paediatr Child Health* 2010; 46: 2-4.

British Paediatric Surveillance Unit (BPSU)

Verity C, Winstone AM, Stellitano L, Krishnakumar D, Will R, McFarland R. The clinical presentation of mitochondrial diseases

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German Paediatric Surveillance Unit (ESPED)

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Further publications can be found at www.inopsu.com.



INoPSU conference, Dublin, Ireland, October 2010

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
- 87% data completion rate

Study ideas

Bronchiectasis
Celiac disease
Childhood tuberculosis
Chylothorax
Congenital syphilis
Fatal and near-fatal asthma
Gonorrhoea, syphilis, chlamydia and trichomonas infections
HIV infections
Hallucinations with psychostimulants
Hypernatremia
Idiopathic intracranial hypertension
Lead levels in children
Life-threatening events / unexplained deaths (first day of life)
Marijuana-induced psychosis
Moderate and severe encephalopathy
Neonatal *Listeria* infections
Rett syndrome
Systemic lupus erythematosus
Texting-related injuries
Underdiagnosed cyanotic congenital heart disease

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