

2013 Results

CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM





Mission

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.

Active surveillance protects patients



Warns

of emergent public health issues

- ▶ Interim use of antiviral medications during pandemic H1N1 influenza
- ▶ CA-MRSA, commonly presenting as skin/soft tissue infections
- ▶ Potential melamine contamination in milk formula products

Identifies

product safety hazards

- ▶ Energy drink health hazards; need to display nutritional/caffeine information
- ▶ Bowel perforations from magnet ingestion; data informed ban from Health Canada
- ▶ Improper use of seat belts; data informed provincial and territorial legislation

Mobilizes

knowledge on possible adverse events

- ▶ Suspected ADRs reported to Health Canada; ADR tips of the month inform paediatricians
- ▶ Medication shortages in paediatrics and problems with therapy after withdrawal of medications
- ▶ Referral patterns of patients with adverse events following immunization or contraindications to vaccinations

Informs

new policies and guidelines

- ▶ Policies/return-to-play protocols to manage patients with concussions
- ▶ Neonatal screening guidelines from MCAD and neonatal hyperbilirubinemia study results
- ▶ Vitamin K injections shown to be best prevention for hemorrhagic disease of the newborn

ADR: adverse drug reaction; CA-MRSA: community-associated methicillin-resistant Staphylococcus aureus infections; MCAD: medium-chain acyl-coenzyme A dehydrogenase deficiency

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Acknowledgements

The key strength of the Canadian Paediatric Surveillance Program (CPSP) is its commitment to improve the health of children and youth in Canada and around the world. This focus 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, the principal investigators who design studies and analyze the data to provide knowledge and educational solutions, or the guidance of the Steering Committee members. We thank them all.

We also thank IMPACT (Immunization Monitoring Program ACTive) centres for their role in verifying the acute flaccid paralysis study data and for their support of the CPSP.

The strong partnership between the Canadian Paediatric Society and the Public Health Agency of Canada 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 support 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 2013 from the Public Health Agency of Canada, Health Canada's Therapeutic Effectiveness and Policy Bureau, and the following non-governmental sources:

- IWK Health Centre – Division of Neonatal-Perinatal Medicine
- New Investigator Fund, Hamilton Health Sciences
- Novartis Pharmaceuticals Canada Inc.
- PSI Foundation
- SickKids Foundation

Foreword

Federal Minister of Health

The Honourable Rona Ambrose

I am pleased to introduce this year's Canadian Paediatric Surveillance Program report. This report provides national surveillance information on rare diseases and conditions among Canadian children and youth.

Surveillance is a powerful tool to help prevent and fight disease. Improving our collective understanding of the burden of disease in Canada is an important first step towards taking action to reduce the demands on families and the health care system.

Monitoring through this program provides data that are useful to numerous stakeholders. For example, health care practitioners can draw on timely and practical information to educate their patients, communities can benefit from knowing how young Canadians are doing, and decision-makers can use data to inform public health policies and programming.

The success of this year's studies would not have been achieved without the participation of the over 2500 paediatricians across Canada. Your contribution is a reminder that we need to continue working together to promote healthy living and reduce the risk factors that lead to greater health problems.

We all have a role to play in helping give young Canadians a good start in life. The Public Health Agency of Canada is proud to have worked with the Canadian Paediatric Society on this initiative, which has helped to strengthen our national surveillance capacity. By joining this effort, we're making an important contribution towards improving the health of young Canadians.



Deputy Chief Public Health Officer of Canada

Dr. Gregory Taylor

On behalf of the Public Health Agency of Canada, I commend the Canadian Paediatric Surveillance Program for its contributions to the health of Canadian children and youth.

The program's monitoring and data on rare diseases and conditions help us determine the burden of disease and potential interventions we can take. It also informs our policies and supports our objective to turn research results into action.

Surveillance plays a crucial role in the fight against disease. Every year, the program gathers data from over 2500 paediatricians and other specialists, who work with children every day. Thanks to this collaborative initiative between the Canadian Paediatric Society and the Public Health Agency of Canada, CPSP data can be accessed and used to improve our collective knowledge and better inform patients. Significantly, communities also benefit, as reports like this help us get a clearer picture of the needs of children and youth, right across the country.

I thank the Canadian Paediatric Society for its leadership and dedication to ensuring decision-makers nationwide have this information in their hands. Together, we're building a healthier population, ensuring our children have the best possible start in life.



President of the Canadian Paediatric Society

Dr. Andrew Lynk

As a community paediatrician living in a rural area, the Canadian Paediatric Surveillance Program offers me the opportunity to be part of a large network of paediatricians, all working towards the same goal: advancing knowledge and, ultimately, better protection and care for our children and youth.



The CPSP continues to tackle new studies and surveys that have tremendous public health implications. Over the years, CPSP study results have: informed policies, position statements and bans on unsafe products; identified potential adverse events; and alerted us to potential health risks due to events occurring in other countries.

A new study began in March 2013 to document the incidence of severe alcohol intoxication in Canadian adolescents. Surveillance of heavy alcohol use among this group is crucial in assisting public health efforts on at-risk populations and has the potential to inform legislation on licensing and minimum drinking age laws.

We are also tracking serious adverse drug reactions, Kawasaki disease, early-onset major depressive disorders, and sudden unexpected death in epilepsy, among others. Recently, for the first time, I diagnosed a child with a periodic fever syndrome, thanks to reading about it in a CPSP publication.

I encourage all members of the Canadian Paediatric Society to remain active participants in the CPSP and to continue to use the results generated from our surveillance studies to improve care and inform advocacy. Go to the CPSP website for more detailed information. Together we are stronger.

CPSP Chair

Dr. Kimberly Dow

Part of a successful surveillance program is taking the results from studies and one-time surveys and disseminating knowledge to front-line health care providers. In 2013, the CPSP and investigators did just that, through many national and international presentations and peer-reviewed articles in journals such as *Brain Injury*, *Canadian Journal of Infectious Diseases & Medical Microbiology*, *Pediatrics*, and *Paediatrics & Child Health*. I encourage you to visit the CPSP website (www.cpsp.cps.ca) regularly to access recent publications. Your contributions have been instrumental in the successful publication of these findings.



As CPSP Chair, I cannot emphasize enough how important it is for us, as paediatricians, to take part in this national surveillance program. We need your help in keeping our response rates high. Each month, the program is asking you to diligently complete your monthly report form, including reporting no cases seen. A nil report is very important in active surveillance, as the program cannot assume that no reply means there were no cases.

Study and one-time survey topics span a wide range and affect all of our practices at some point. In 2013, a variety of new studies began: Kawasaki disease, severe alcohol intoxication in adolescents, childhood tuberculosis, and unexpected sudden infant death and severe apparent life-threatening events in the early postnatal period.

Again, I wish to thank all Canadian paediatricians for participating in the CPSP. The CPSP Steering Committee looks forward to receiving your ideas for new studies and surveys throughout the coming years.

CPSP Steering Committee

Kimberly Dow, MD (Chair)	Canadian Paediatric Society
Peter Buck, DVM, MSc	Centre for Food-borne, Environmental and Zoonotic Infectious Diseases, Public Health Agency of Canada
Claude Cyr, MD	Canadian Paediatric Society
Marie Adèle Davis, MBA	Canadian Paediatric Society
Ciaran Duffy, MB	Paediatric Chairs of Canada
Kevin Gordon, MD	Canadian Association of Child Neurology (Liaison)
Danielle Grenier, MD	Canadian Paediatric Society
W. James King, MD	Canadian Paediatric Society
Jonathon Maguire, MD	Canadian Paediatric Society
Dorothy Moore, MD	IMPACT (Immunization Monitoring Program ACTive) (Liaison)
Paul Muirhead, LL.M.	Consultant
Jeff Scott, MD	Canadian Paediatric Society
Dorcas Taylor, MSc	Centre for Communicable Diseases and Infection control, Public Health Agency of Canada
Paul Thiessen, MD	Canadian Paediatric Society
Lesley Ann Turner, MD	Canadian College of Medical Geneticists (Liaison)
Kim Tytler	Canadian Paediatric Society
Anne-Marie Ugnat, PhD	Centre for Chronic Disease Prevention, Public Health Agency of Canada

In November 2013, **Jeff Scott** completed his term as a representative of the Canadian Paediatric Society on the CPSP Steering Committee. Jeff also previously served as a liaison for the Council of Chief Medical Officers of Health. We sincerely thank him for his hard work over the past years and wish him all the best in future endeavours.

CPSP Working Group

Kim Tytler (Chair)	Canadian Paediatric Society
Marie Adèle Davis, MBA	Canadian Paediatric Society
Danielle Grenier, MD	Canadian Paediatric Society
Melanie Khalil, BA	Canadian Paediatric Society
Anne-Marie Ugnat, PhD	Centre for Chronic Disease Prevention, Public Health Agency of Canada

Publications 2009–2013

Published papers related to studies and one-time surveys

(For a complete list with hyperlinks, see www.cpsp.cps.ca/publications/published-papers-related-to-studies.)

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

Child maltreatment

Head injury secondary to suspected child maltreatment: Results of a Canadian national surveillance program. Bennett S, Ward M, Moreau K, Fortin G, King J, MacKay M, Plint A. *Child Abuse Negl* 2011;35(11):930–6

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

Concussion management

Concussion management by paediatricians: A national survey of Canadian paediatricians. Gordon KE, Do MT, Thompson W, McFaul S. *Brain Inj* 2013 Dec 19 (Epub ahead of print). doi:10.3109#02699052.2013.862740

Congenital myotonic dystrophy

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

Congenital myotonic dystrophy: Canadian population-based surveillance study. Campbell C, Levin S, Siu VM, Venance S, Jacob P. *J Pediatr* 2013;163(1):120-5. Epub 2013 Feb 14. pii: S0022-3476(12)01559-4. doi: 10.1016/j.jpeds.2012.12.070

Congenital rubella syndrome

Rubella elimination: The Canadian experience. Macey JF, Tam T, Lipskie T, Tipples G, EisBrenner T. *J Infect Dis* 2011;204:S585–92

Eating disorders

Incidence and age-specific presentation of restrictive eating disorders in children – A Canadian Paediatric Surveillance Program study. Pinhas L, Morris A, Crosby RD, Katzman DK. *Arch Pediatr Adolesc Med* 2011;165(10):895–9. doi:10.1001/archpediatrics.2011.145

Food allergy

Canadian allergists' and nonallergists' perception of epinephrine use and vaccination of persons with egg allergy. Desjardins M, Clarke A, Alizadehfard R, Grenier D, Eisman H, Carr S, et al. *J Allergy Clin Immunol: In Practice* 2013;1:289–94

Kernicterus / neonatal hyperbilirubinemia

Incidence of chronic bilirubin encephalopathy in Canada, 2007–2008. Sgro M, Campbell DM, Kandasamy S, Shah V. *Pediatrics* 2012;130(4):e886–90. doi:10.1542/peds.2012-0253

Acute neurological findings in a national cohort of neonates with severe neonatal hyperbilirubinemia. Sgro M, Campbell D, Barozzino T, Shah V. *J Perinatol* 2011;31(6):392–6. Epub 2010 Dec 9; doi:10.1038/jp.2010.137

Medium-chain acyl-CoA dehydrogenase deficiency

Incidence of medium-chain acyl-CoA dehydrogenase deficiency in Canada using the Canadian Paediatric Surveillance Program: Role of newborn screening. Prasad C, Speechly KN, Dyak S, Rupar CA, Chakraborty P, Kronick JB. *Paediatr Child Health* 2012;17(4):185–9

Methicillin-resistant *Staphylococcus aureus* (MRSA)

Clinical characteristics of pediatric patients hospitalized with methicillin-resistant *Staphylococcus aureus* in Canadian hospitals from 2008 to 2010. Leifso KR, Gravel D, Mouchili A, Kaldas S, Le Saux N. *Can J Infect Dis Med Microbiol* 2013;24(3):e53–6

Non-type 1 diabetes mellitus

Differing clinical features in Aboriginal vs. non-Aboriginal children presenting with type 2 diabetes. Amed S, Hamilton JK, Sellers EAC, Panagiotopoulos C, Hadjiyannakis S, Shah BR, Booth GL, Laubscher TA, Dannenbaum D, Dean H. *Pediatr Diabetes* 2012;13(6):470–5. doi:10.1111/j.1399-5448.2012.00859.x

Risk factors for medication-induced diabetes and type 2 diabetes. Amed S, Dean H, Sellers EAC, Panagiotopoulos C, Shah BR, Booth GL, et al. *J Pediatr* 2011;159(2): 291–6. doi:10.1016/j.jpeds.2011.01.017

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

Paediatric myasthenia

Clinical characteristics of paediatric myasthenia: A surveillance study. VanderPluym J, Vajsar J, Jacob FD, Mah JK, Grenier D, Kolski H. *Pediatrics* 2013;132(4):e939–44. doi:10.1542/peds.2013-0814

Severe combined immunodeficiency

Severe combined immunodeficiency (SCID) in Canadian children: A national surveillance study. Rozmus J, Junker A, Thibodeau ML, Grenier D, Turvey SE, Yacoub W, Embree J, Haddad E, Langley JM, Ramsingh RM, Singh V-A, Long R, Schultz KR. *J Clin Immunol* 2013;33:1310–6

Transfusion-related acute lung injury

Transfusion-related acute lung injury in the Canadian paediatric population. Gauvin F, Robillard P, Hume H, Grenier D, Whyte R, Webert KE, Fergusson D, Lau W, Froese N, Delage G. *Paediatr Child Health* 2012;17(5):235–9

CPSP Highlights and Commentaries published in 2013 in *Paediatrics & Child Health*

(For a complete list with hyperlinks, see www.cpsp.cps.ca/publications/cpsp-highlights.)

Having some drinks: A normal part of growing up or a signal of a larger problem? Acker A, Thomas K. *Paediatr Child Health* 2013;18(10):512

From bruises to brain injury: The physician's role in the assessment of inflicted traumatic head injury. Ward MGK, King WJ, Bennett S. *Paediatr Child Health* 2013;18(8):423–4

The unexpected: Sudden infant death in the postnatal period. Feldman K. *Paediatr Child Health* 2013;18(7):360

Fragile X syndrome: Are paediatric health care providers missing the diagnosis? Aubertin G. *Paediatr Child Health* 2013;18(5):251–2

A 'knock on the noggin'. Gordon K, Do MT, Thompson W, McFaul S, Taylor B. *Paediatr Child Health* 2013;18(3):142

Avoiding hypotonic solutions in paediatrics: Keeping our patients safe. Beck CE, Choong K, Puligandla PS, Hartfield D, Holland J, Lacroix J, Friedman JN. *Paediatr Child Health* 2013;18(2):94–5

Obesity hypoventilation syndrome: A different beast. Folman R, Grenier D, Birken C, Campisi P, Do MT, Forte V, MacLusky I, McCrindle BW, Narang I, Witmans M. *Paediatr Child Health* 2013;18(1):36

Presentations in 2013

(For a complete list with hyperlinks, see www.cpsp.cps.ca/publications/presentations.)

National

Concussion management

Concussion management by Canadian paediatricians: A national survey. Gordon KE, Do MT, Thompson W, McFaul S. Canadian Paediatric Society Annual Conference, Edmonton, in June (oral)

Conversion disorder

Understanding conversion disorder: Does mind rule body or does body rule mind? Krasnik C, Grant C. Canadian Paediatric Society Annual Conference, Edmonton, in June (oral)

Canadian Paediatric Surveillance Program (CPSP) conversion disorders in children and youth: Preliminary data from a national survey of clinical features and treatment outcomes. Krasnik CE, Grant C. Canadian Paediatric Society Annual Conference, Edmonton, in June (oral)

Growth charts

A national survey of the opinions of Canadian paediatric health care providers regarding the WHO and CDC growth charts. Lawrence SE, Cummings EA, Chanoine JP, Metzger DL, Palmert MR, Sharma AK, Rodd CJ. Canadian Paediatric Society Annual Conference, Edmonton, in June (poster)

Kernicterus / neonatal hyperbilirubinemia

Surveillance of severe neonatal hyperbilirubinemia in Canada: 2010–2013. Sgro M, Kandasamy S, Campbell DM, Ofner M, Shah V. Canadian Paediatric Society Annual Conference, Edmonton, in June (poster)

Methadone exposure

Accidental or intentional methadone ingestion in children and infants: A national pulse of the issue among Canadian paediatricians. Lewington LE, Marcus SM, Shaffer C, Vulliamy A, Ornstein A. Canadian Paediatric Society Annual Conference, Edmonton, in June (poster)

Neonatal sepsis and meningitis

Early-onset neonatal sepsis and meningitis – Neonates less than seven days of age. Sgro M, Tran D, Lee SK, Sankaran K, Yudin M, Campbell D. Canadian Paediatric Society Annual Conference, Edmonton, in June (poster)

Respiratory syncytial virus infections

Interim results for the Canadian paediatric surveillance project – Respiratory syncytial virus infections in paediatric transplant recipients. Robinson J, Allen U, Grenier D. Canadian Paediatric Society Annual Conference, Edmonton, in June (poster)

International

Acute flaccid paralysis

Comparison of acute flaccid paralysis surveillance by the International Network of Paediatric Surveillance Units. Desai S, Smith T, Grenier D, Alpeter E, Beeli D, Dickson N, Phillips A, Thorley B, Sabbe M, Zurynski Y. International Congress of Pediatrics, Melbourne, in August (poster)

Concussion management

Concussion management by Canadian paediatricians: A national survey. Gordon K, Grenier D, Do MT, Thompson W, McFaul S. International Congress of Pediatrics, Melbourne, in August (poster)

Conversion disorder

Conversion disorders in children and youth: A national survey of clinical features and treatment outcomes. Krasnik CE, Grant C. International Congress of Pediatrics, Melbourne, in August (poster)

Presentations in 2013

Kernicterus / neonatal hyperbilirubinemia

Comparing rates of severe neonatal hyperbilirubinemia in three western, industrialized populations: Canada, The United Kingdom and Ireland, and Switzerland. Sgro M, Kandasamy S, Ofner M, Campbell DM, Grenier D, Simone L. International Congress of Pediatrics, Melbourne, in August (poster)

Surveillance of severe neonatal hyperbilirubinemia in Canada: 2011–2013. Sgro M, Kandasamy S, Campbell D, Shah V, Grenier D, Ofner M. International Congress of Pediatrics, Melbourne, in August (poster)

Neonatal sepsis and meningitis

Early onset neonatal sepsis and meningitis: Neonates less than seven days of age. Sgro M, Tran D, Lee SK, Sankaran K, Yudin MH, Grenier D, Campbell DM. International Congress of Pediatrics, Melbourne, in August (poster)

Persistent albuminuria in the paediatric population with type 2 diabetes mellitus

Minimum prevalence of persistent albuminuria in youth <18 years of age with type 2 diabetes mellitus: A Canadian Paediatric Surveillance Program study. Sellers E, Hadjiyannakis S, Amed S, Dart A, Dyck R, Hamilton JK, Langlois V, Panagiotopoulos C, Ugnat A-M, Dean HJ. American Diabetes Association's Scientific Sessions, Chicago, in June (poster)

Clinical factors associated with persistent albuminuria in youth-onset type 2 diabetes mellitus: A Canadian Paediatric Surveillance Program study. Sellers E, Hadjiyannakis S, Dean HJ, Dart A, Dyck R, Hamilton JK, Langlois V, Panagiotopoulos C, Ugnat A-M, Amed S. American Diabetes Association's Scientific Sessions, Chicago, in June (poster)

Surveillance – General

Public health impacts of INoPSU data – International perspectives. Grenier D. Workshop: International Network of Paediatric Surveillance Units – The power of international collaboration to study rare diseases. International Congress of Pediatrics, Melbourne, in August (oral)

Surveillance as a tool to serve Aboriginal health needs. Grenier D, Ugnat A-M, Laffin Thibodeau M, Davis MA. International Congress of Pediatrics, Melbourne, in August (poster)

Surveillance as a tool to serve Aboriginal health needs. Grenier D, Parkin P, Sellers E, Amed S. International Meeting on Indigenous Child Health, Portland OR, in April (poster)

Surveillance at Work

Overview

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

According to Statistics Canada, the Canadian population on July 1, 2013 was an estimated 35,158,304, with 7,853,129 individuals 0–19 years of age, which represents approximately 22% of the population. Although individually uncommon, rare diseases affect hundreds of thousands of Canadian children and youth and typically have lifelong impacts. The incidence of many rare disorders is unknown, and yet is essential for improved clinical care, advocacy and health service planning.

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 scientific and 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 infectious disease specialists. The program also offers an opportunity for international collaboration with other paediatric surveillance units worldwide, through the International Network of Paediatric Surveillance Units (INoPSU).

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 the 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. Case ascertainment is undertaken by comparing a few selected study results with cases reported to the hospital Discharge Abstract Database of the Canadian Institute for Health Information (CIHI) and by investigating duplicate reports and comparing data with related programs or centres. To date, case ascertainment has been excellent.

Reporting

The check-off form, listing the conditions currently under surveillance, is distributed 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 there were no cases. In October 2011, the program launched eCPSP, an electronic platform giving participants the opportunity to receive their monthly forms online. By December 2013, 65% of program participants were signed up for electronic reporting.

Participants report all cases meeting the case definitions, including suspect or probable cases. This sometimes leads to duplicate reports but avoids

TABLE 1 – Initial response rates (%) and number of participants for 2013

Provinces/territories	Reporting rates (%)	Number of participants
Alberta (AB)	77	335
British Columbia (BC)	79	256
Manitoba (MB)	80	118
New Brunswick (NB)	83	29
Newfoundland and Labrador (NL)	87	53
Nova Scotia (NS)	86	94
Northwest Territories (NT)	100	2
Nunavut (NU)	100	2
Ontario (ON)	78	956
Prince Edward Island (PE)	99	8
Quebec (QC)	79	560
Saskatchewan (SK)	72	55
Yukon (YT)	100	1
Canada	80	2469

Surveillance at Work

missed cases. The list of studies conducted by the program since 1996 can be accessed at www.cpsp.cps.ca/surveillance.

Confidentiality is maintained by using only non-nominal patient information, such as the date of birth and sex of the child. 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 manager contacts the respondent on behalf of the investigator.

Participants who do not reply every month receive reminders. In addition, information on the monthly compliance rates and the number of cases reported is distributed quarterly to all participants to keep them informed of progress. In 2013, the national reporting rate was 80% (Table 1) and the response rate for completion of detailed questionnaires, 84% (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 2013, the majority of participants (95%) 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 2013. As studies come and go, the workload shifts to different subspecialties. Through the years, studies with national collaborative networks have been very successful. The 2013 studies with the most reports were periodic fever syndromes and conversion disorder.

The CPSP is extremely grateful that the majority of participants faithfully complete the detailed questionnaires subsequent to reporting cases. This step 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, the names of participants who completed the initial reporting forms for all months in 2013 and/or returned one or more detailed questionnaires were entered in draws for various prizes.

Investigators' corner

Through timely, active surveillance, the CPSP provides investigators with an innovative means of obtaining non-nominal, national data on low-frequency diseases and conditions from over 2500 participants. The program

TABLE 2 – 2013 detailed questionnaire completion rates as of May 1, 2014

Studies/conditions	Reported cases*	Pending	% Completion rate
Acute flaccid paralysis	41	1	98
Adverse drug reactions – serious and life-threatening	38	6	84
Childhood tuberculosis	17	3	82
Conversion disorder in children and youth	59	14	76
Early-onset major depressive disorder	9	2	78
Fragile X syndrome	21	3	86
Kawasaki disease	51	16	69
Neonatal hyperbilirubinemia – severe (2011–2013)	20	2	90
Periodic fever syndromes	63	9	86
Respiratory syncytial virus infections in paediatric transplant patients	8	0	100
Severe alcohol intoxication in adolescents	26	2	92
Unexpected sudden infant death and severe apparent life-threatening events in the early postnatal period	13	1	92
Total number of cases (all studies)	367	59	84

* Excluding duplicate and excluded cases

TABLE 3 – Number of cases reported by respondents in 2013

Number of cases	% Respondents
0	95.0
1–5	4.8
6–10	0.1
>10	0.1

is committed to a high case-ascertainment rate and, due to follow-up reminders to non-respondents, obtains a response rate of 84% 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 to follow the “format for submission”, available on the CPSP website at www.cpsp.cps.ca/apply-proposez. 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, www.cpsp.cps.ca, or to contact the manager of surveillance 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 to identify the prevalence of a problem or answer a specific question. Once approved by the CPSP Steering Committee, the one-time survey is sent to all participants with the monthly initial reporting form. Collected results are forwarded to the investigator for data analysis.

Results of the 2013 one-time survey questions are found on pages 43–45, and the list of surveys completed to date can be accessed at www.cpsp.cps.ca/surveillance/one-time-surveys.

Glossary of terms for tables of cases in each study results

Reported: Reports of cases received

Duplicates: Cases reported by more than one participant

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 2013



Dr. Shalini Desai
Acute flaccid paralysis



Margaret Zimmerman
*Adverse drug reactions –
serious and life-threatening*



Dr. Shaun Morris
Childhood tuberculosis



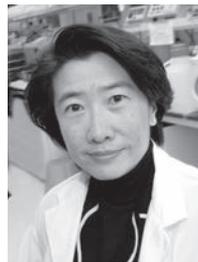
Dr. Christina Grant
*Conversion disorder in
children and youth*



Dr. Daphne Korczak
*Early-onset major
depressive disorder*



Dr. Gudrun Aubertin
Fragile X syndrome



Dr. Rae Yeung
Kawasaki disease



Dr. Michael Sgro
*Neonatal
hyperbilirubinemia –
severe (2011–2013)*



Dr. Paul Dancey
Periodic fever syndromes



Dr. Joan Robinson
*Respiratory syncytial virus
infections in paediatric
transplant patients*



Dr. Amy Acker
*Severe alcohol
intoxication in
adolescents*



Dr. Kayla Feldman
*Unexpected sudden infant
death and severe apparent
life-threatening events in
the early postnatal period*

Surveillance Studies in 2013

Acute flaccid paralysis

January 1996 to December 2016

S Desai, T Smith

Highlights 2013

- Canada conducts acute flaccid paralysis (AFP) surveillance in the under 15 population to monitor for polio in light of ongoing transmission of wild poliovirus in countries around the world.
- All 24 cases of AFP confirmed in 2013 were thoroughly investigated and no cases were diagnosed with polio. The most common diagnosis was Guillain-Barré syndrome (GBS).
- The AFP surveillance case report form is currently being updated with an aim of improving Canada's ability to meet the World Health Organization (WHO) surveillance performance objectives.

Background and objectives

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance.

Case definition

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

Results

There were 41 notifications of AFP through the CPSP to the Public Health Agency of Canada with onset in 2013, and the detailed questionnaire completion rate was 95%.

At the time of analysis, there were 24 confirmed cases of AFP. No cases of polio were identified. Approximately 37% of all reports came from the CPSP network and 63% from the Canadian Immunization Monitoring Program ACTIVE (IMPACT). Excluded reports included three cases that did not meet the case definition, one case that was lost to follow-up, and one case that was transferred to an IMPACT hospital which then took on reporting responsibility. The 24 confirmed cases represent a non-polio AFP detection rate of 0.42/100,000 in children younger than 15 years of age (Table 2). As this study is ongoing, delays in reporting may have occurred. Therefore, figures will be adjusted accordingly once detailed case report forms have been received.

Reported	Duplicates	Excluded	Pending	Confirmed
41	2	5	10	24

In 2013, the age of confirmed cases of AFP ranged from 1 to 14 years with a mean of 7.5 years (95% CI 5.8–9.2) which is consistent with the mean age observed in previous years of the study (6.8 [95% CI 6.5–7.1]). A total of 62% of AFP cases were male and 38% were female.

Among the AFP cases reported in 2013, documentation of age-appropriate polio immunization was provided for 8 cases (33%), 9 cases (38%) were recorded as “up-to-date” with no further information, and the remaining 7 cases (29%) included no information on immunization. Vaccine uptake rates of inactivated poliovirus vaccine (IPV) in Canada are estimated to be approximately 95% for four doses or more among 7-year-olds, based on preliminary data from the 2011 Childhood National Immunization Coverage Survey (unpublished data).

Investigation for polio virus, other enteroviruses or *Campylobacter*

Virological investigation included testing of stool specimens for 5 cases (21%), cerebrospinal fluid (CSF) for 18 cases (75%), and throat swabs for 4 cases (17%). Where stool was collected, 80% were considered adequate, that is, having been taken within 14 days of the onset of paralysis. For the remaining cases, stool collection occurred later, and the sensitivity of enterovirus isolation would have been lower. Overall, of the 24 confirmed

Surveillance Studies in 2013

cases, 17% (n=4) of cases had an adequate stool sample collected within 14 days of the onset of paralysis (Table 2). None of the samples collected in 2013 were positive for polioviruses. Testing was also conducted for *Campylobacter* in four cases (17%) and this bacterium was not isolated in any of the samples.

Neurological investigations

In 2013, all 24 cases underwent at least one type of neurological investigation (CSF examination, nerve conduction studies/electromyography, MRI/CT scan). The most frequently used investigative methods were CSF examination (92%) and MRI/CT scans (88%). Of these tested cases, approximately 95% had abnormal CSF chemistry results, 82% had abnormal electromyography and/or nerve conduction studies, and 62% had an abnormal MRI or CT scan. As observed in previous years, the majority of AFP cases (n=20, 83%) were diagnosed as GBS, two of which were Miller-Fisher variants. The remaining four cases were diagnosed as acute disseminated encephalomyelitis (n=2) and transverse myelitis (n=2).

Hospitalization and outcome

The majority of AFP cases in 2013 were hospitalized (n=23). Information on length of hospital stay was available for 19 cases and ranged from 1 to 32 days with a mean of 11 days (95% CI 7.4–15.0) which was consistent with the mean length of hospital stay seen in previous years of the study (13 [95% CI 12.1–14.5]). Outcome at the time of the initial report was documented in 22 cases (92%): 2 (9%) fully recovered, 18 (82%) partially recovered with residual weakness or paralysis and 2 (9%) were not recovered. Only 6 cases (25%) had clinical outcomes reported at 60 days, including 2 cases who had fully recovered and 4 with partial recovery (i.e., some residual weakness or paralysis).

Discussion

The majority of cases of poliomyelitis are asymptomatic. A small percentage of cases, approximately 4% to 8%, may manifest as a nonspecific 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 infection. If poliomyelitis is suspected, further consultation with a neurologist and infectious diseases specialist would be prudent.

Until polio is eradicated globally, AFP surveillance is a core program that assists in monitoring Canada's polio-free status. This surveillance system is also useful in identifying other causes of acute flaccid paralysis that may warrant further investigation and public health intervention.

The Public Health Agency of Canada, in collaboration with the CPSP, has begun to revise the AFP case report form with the aim of launching a new form in 2015. Issues with the current form had been informally noted in recent years by data providers, case reviewers, and data analysts related to length, clarity and overall usefulness of the information collected. The current data collection tool also results in limitations in data analysis due to missing or unknown information (e.g., immunization status, follow-up duration after onset of paralysis). In addition, findings

TABLE 2 – Measure of WHO AFP surveillance targets in Canada, 1996–2013

Year	Number of cases	Incidence rate*	% with adequate stool sample†	% with 60 days follow-up‡
1996	27	0.45	18.5	70.4
1997	35	0.59	28.6	45.7
1998	43	0.72	25.6	46.5
1999	60	1.01	33.3	33.3
2000	64	1.09	45.3	37.5
2001	52	0.89	36.5	38.5
2002	44	0.75	31.8	34.1
2003	44	0.76	34.1	22.7
2004	38	0.66	44.7	28.9
2005	53	0.93	26.4	32.1
2006	39	0.69	20.5	43.6
2007	50	0.89	42.0	46.0
2008	42	0.75	33.3	42.9
2009	59	1.05	30.5	49.2
2010	47	0.84	34.0	55.3
2011	43	0.76	32.6	48.8
2012	32	0.57	46.9	34.4
2013	24	0.42	16.7	25.0

* Incidence rate per 100,000 population; WHO target: 1.0/100,000

† Adequate stool sample refers to one stool sample taken within 14 days of paralysis onset; WHO target: 80%

‡ WHO target: 80%

from a recent international comparison of AFP surveillance also highlighted areas for improvement within the Canadian form. The update of the form also provides an opportunity to engage stakeholders in discussions on AFP surveillance and identify measures that can be taken in Canada to address gaps related to the ability to meet the AFP surveillance performance targets developed by WHO.

Conclusion

- The most common diagnosis of AFP was GBS.
- A stool sample collected within 14 days of the onset of paralysis is important for ruling out poliomyelitis.

Publications and presentations

Desai S, Smith T, Thorley BR, Grenier D, Dickson N, Altpeter E, SPSU Committee, Sabbe M, Elliot E, Zurynski Y. Comparison of acute flaccid paralysis surveillance by the International Network of Paediatric Surveillance Units. International Congress of Pediatrics, Melbourne, August 2013. (Poster presentation)

Acknowledgements

The contribution of Jenne Cunliffe is greatly appreciated.

References

Available upon request from the CPSP office

Principal investigator

Shalini Desai, MD, FRCPC, Centre for Immunization and Respiratory Infectious Diseases, Public Health Agency of Canada; shalini.desai@phac-aspc.gc.ca

Adverse drug reactions – serious and life-threatening

January 2004 to December 2016

M Zimmerman

Highlights 2013

- The study confirmed 21 suspected paediatric cases of adverse reactions (ARs). This represents the lowest number of confirmed cases per year since 2007.
- Product groups most commonly associated with suspected ARs were antibacterial agents, immunosuppressants and corticosteroids for systemic use.
- In 2013, the majority of the AR reports described skin and subcutaneous disorders, a finding consistent with the trend observed since 2004.

Background and objectives

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance.

Case definition

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

Reactions to medical devices, blood products (platelets, red cells and single-donor plasma), vaccines, poisonings or self-administered overdoses

Results

From January 1 to December 31, 2013, 38 cases of suspected adverse drug reactions (ADRs) were reported and 21 cases were confirmed as meeting the case definition.

Reported	Duplicate	Excluded	Pending	Confirmed
38	0	6	11	21

Of the 21 confirmed cases, 11 were male and 10 were female, ranging in age from 3 months to 17 years. By age group, the largest number of reports involved children aged up to 5 years (n=10) followed by children aged 6 to 12 years (n=6) and adolescents aged 13 to 17 years (n=5). Table 2 compares the age distribution for confirmed cases over the last seven years.

	2013 (n=21)	2012 (n=31)	2011 (n=31)	2010 (n=34)	2009 (n=51)	2008 (n=40)	2007 (n=45)
Up to 5 years	10	3	10	6	14	15	9
6 to 12 years	6	14	7	16	16	14	16
13 to 17 years	5	14	14	11	21	11	18
Not reported	0	0	0	1	0	0	2

All 21 confirmed cases were classified as serious, with more than one reason for seriousness reported in 8 cases. No deaths were reported in 2013. Table 3 compares the reasons for seriousness over the last seven years.

Information regarding patient outcome was provided for all 21 reports as follows: recovered (n=15); recovering/resolving (n=2); not yet recovered (n=3); and recovered with sequelae (n=1).

The majority of the reports described reactions documented in standard drug references for the suspected health products. The information source used for this determination was the Canadian approved product monograph. When an approved product monograph was not available, the information source was the Compendium of

Pharmaceuticals and Specialties electronic version, the Micromedex™ Drug Information System or the American Hospital Formulary Service™ (AHFS) Drug Information reference. A summary is provided for one report involving a reaction not described in standard drug reference sources.

	2013 (n=21)	2012 (n=31)	2011 (n=31)	2010 (n=32)	2009 (n=45)	2008 (n=35)	2007 (n=41)
Death	0	1	1	0	1	3	2
Life-threatening	6	11	11	6	14	12	9
Hospitalization	19	20	18	19	28	18	19
Disability	1	2	4	2	3	0	0
Medically important condition*	7	13	17	18	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.

A child was found to have asymptomatic bigeminy/trigeminy and premature ventricular contractions on Holter monitor during a sleep study. He had been taking lisdexamfetamine dimesylate at doses of 40 to 60 mg daily for approximately three years. The patient had a history of attention deficit/hyperactivity disorder, Kartagener’s syndrome and conduct disorder. He was taking aripiprazole 5 mg daily concurrently along with inhaled salbutamol, fluticasone and tobramycin. ECG readings returned to normal following the discontinuation of lisdexamfetamine.

Suspect health products

Table 4 lists the 22 suspect health products described in the 21 reports, sorted by the number of reports received per individual product. In 18 reports a single product was suspected of causing the reaction, and in four reports two suspect products were provided. The classes of health product most frequently suspected of causing the adverse reaction(s) were antibacterial agents (n=6), followed by immunosuppressants (n=5) and corticosteroids (n=3). Two reports each were received for psycholeptics, psychoanaleptics and thyroid therapies.

Suspect health product	# Times reported
Aripiprazole, prednisolone, thiamazole, vancomycin	2 each
Acyclovir, adalimumab, amoxicillin, azathioprine, dapsone, etanercept, gentamicin, ibuprofen, immunoglobulin human, lamotrigine, leflunomide, lenalidomide, lisdexamfetamine dimesylate, methylphenidate, nitrofurantoin, prednisone, sildenafil, sodium phosphate (enema)	1 each

Trends in CPSP reporting (2004–2013)

Since the introduction of this study in January 2004, 489 suspected ADRs have been reported via the CPSP. Due to a change in the lead investigator, data for January to December 2006 are not available and will not be discussed. The number of reports received per year has ranged from 68 (2008) to 38 (2013). Of the 489 reported ADRs, 320 cases were confirmed as meeting the case definition, 56 were excluded as not meeting the case definition, 2 reports were determined to be duplicates, and the remaining 111 are pending. The most common reasons reported for seriousness of confirmed cases were: medically important (n=141), hospitalization or prolonged-hospitalization (n=198), life-threatening (n=90), disability (n=15) and death (n=8). Of note, more than one reason for seriousness is sometimes reported in cases. The majority of the suspected ADRs were previously recognized reactions documented in standard drug references.

Product class	Number of reports	Most frequently reported product in class (number of reports)
Antibacterials for systemic use	104	Amoxicillin (n=22)
Antiepileptics	71	Carbamazepine (n=28)
Psychoanaleptics	52	Methylphenidate (n=17) Atomoxetine (n=17)
Antineoplastics	26	Peg-l-asparaginase (n=7)
Immunosuppressants	25	Infliximab (n=9)
Psycholeptics	21	Risperidone (n=7)
Anti-inflammatory and antirheumatic products	20	Ibuprofen (n=11)
Anesthetics	15	Propofol (n=3)
Sex hormones and modulators of the genital system	11	Ethinyl estradiol/ drospirenone (n=3) Ethinyl estradiol/levonorgestrel (n=3)
Analgesics	10	Acetylsalicylic acid (n=3)

Surveillance Studies in 2013

The AR reports received from the CPSP since January 2004 have involved 187 different health products (167 pharmaceuticals, 15 biologic/biotechnology products, 5 natural health products). Table 5 lists the product classes involving 10 or more CPSP AR reports and the most frequently reported product in the class. Antibacterial agents were reported as the suspect product in 104 reports. Next in frequency were antiepileptics in 71 reports and psychoanaesthetics in 52 reports.

In 2013, the majority of the AR reports described skin and subcutaneous disorders. This finding is consistent with the trend observed since 2004.

Discussion

The classes of health products most frequently suspected of causing the ARs reported in 2013 were antibacterials for systemic use, followed by immunosuppressants and corticosteroids for systemic use. For all reports received through the CPSP since January 2004, antibacterial agents represented the most frequently associated product class, with amoxicillin being the individual product most frequently involved. Antiepileptics and psychoanaesthetics have been the second and third most frequently associated product groups for all reports received. The majority of the suspected ADRs were previously recognized reactions documented in standard drug references.

Health Canada recognizes the need to strengthen information related to paediatric health, as the use of medications to treat children is increasing, and the safety and efficacy of these medications may be significantly different in paediatric patients than in adult patients. The ongoing sharing of safety information through reporting of ARs from various sources such as the CPSP is therefore valuable to Health Canada, as it can provide information on the benefit-risk profile of health products used in children and can result in the implementation of risk mitigation measures when the risks are deemed to outweigh the benefits.

Conclusion

- Since January 2004, a total of 489 cases of suspected paediatric ARs have been reported to the CPSP with 320 cases confirmed as meeting the case definition.
- Product groups most commonly associated with suspected ARs were antibacterials, followed by antiepileptics and psychoanaesthetics.
- Ongoing reporting of ARs is important in determining the benefit-risk profile of health products used in the paediatric population.

Caveat: *Adverse reactions (ARs) 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.*

Acknowledgements

The assistance of Lynn MacDonald is greatly appreciated.

References

Available upon request from the CPSP office

Principal investigator

Margaret Zimmerman, BSc, Patient Safety Section, Marketed Health Products Directorate, Health Canada, Bldg 7, AL 0701C, Tunney's Pasture, Ottawa ON K1A 0K9; tel.: 613-957-2806; fax: 613-948-7996; margaret.zimmerman@hc-sc.gc.ca

Childhood tuberculosis

October 2013 to September 2016

SK Morris, I Kitai, A Al-Azem, G Alvarez, C Archibald, M Baikie, R Consunji-Araneta, V Cook, K Elwood, V Gallant, B Grueger, C Hui, JM Langley, A Miners, J Pernica, N Radziminski, E Rea, M Salvadori, L Sauvé, K Stewart, A Tse-Chang, S Wong, T Wong, D Zielinski

Highlights 2013

- Existing data suggest that childhood tuberculosis (TB) is not distributed evenly across the country and there are some areas and populations with very high rates while others are very low.
- The incidence of both multi-drug-resistant TB and extensively drug-resistant TB is increasing in many parts of the world but is unknown in Canada.
- Eight confirmed cases were identified in the first three months of the study, seven were Aboriginal and one was born overseas.

Background and objectives

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance.

Case definition

A new active or re-treatment case of TB disease in a patient under the age of 15 years

Proven TB disease

1. Laboratory-confirmed

Isolation of *M tuberculosis* complex from any clinical specimen:

Positive culture **or** positive nucleic acid amplification test (NAAT), specifically *M tuberculosis*, *M africanum*, *M canetti*, *M caprae*, *M microti*, *M pinnipedii* or *M bovis* (excluding *M bovis* BCG strain)

2. Clinically confirmed

Probable intrathoracic	Probable extrapulmonary – non-pleural
Signs and symptoms, histology suggestive of TB or close contact with an infectious source case	Signs and symptoms, histology or findings on diagnostic radiology consistent with TB
Chest radiography consistent with intrathoracic TB disease	
and at least one of the following: <ul style="list-style-type: none"> A positive clinical response to anti-TB treatment Documented exposure to active case of infectious <i>M tuberculosis</i> Immunological evidence of <i>M tuberculosis</i> infection: <ul style="list-style-type: none"> Positive TB skin test (TST) or positive interferon gamma release assay (IGRA) 	

Presumed TB disease

Treatment for suspected TB disease at any site with at least three anti-TB drugs

Cases are identified as “new” or “re-treatment” based on the following criteria:

- New active case of tuberculosis disease:** No documented evidence or history of previously active tuberculosis
- Re-treatment case of tuberculosis:**
 - Documented evidence or adequate history of previously active TB that was declared cured or treatment completed by current standards and
 - At least a six-month interval since the last day of previous treatment and
 - Diagnosis of a subsequent episode of TB that meets the active TB case definition

or

 - Documented evidence or adequate history of previously active TB that cannot be declared cured or treatment completed by current standards and
 - Inactive disease for six months or longer after the last day of previous treatment and
 - Diagnosis of a subsequent episode of TB that meets the active TB case definition

Surveillance Studies in 2013

Exclusion criteria

- Isolation of another pathogen, including atypical mycobacteria
- Patient arriving in Canada on TB treatment for presumed TB but for whom treatment is stopped because subsequent work-up in Canada suggests no TB
- Patient with latent TB (TST- or IGRA-positive but no clinical or radiologic abnormality)

Results

TB is caused by the bacterium *Mycobacterium tuberculosis* and less commonly *Mycobacterium bovis* and remains an infection of tremendous clinical and public health importance in Canada. The diagnosis and management of tuberculosis in children, especially in children under 5 years of age, are often particularly complex. The importance of studying and understanding the epidemiology and clinical history of childhood tuberculosis in Canada is underlined by: changes in immigration patterns from tuberculosis endemic regions; an increase in immune-compromised children due to underlying disease, treatment or transplants; and rapidly changing patterns of microbial resistance.

Reported	Duplicate	Excluded	Pending	Confirmed
17	2	1	6	8

The CPSP childhood tuberculosis study was launched in late 2013, and 17 cases were reported, of which eight have been confirmed as unique cases meeting inclusion criteria. While it is too early to fully analyze the cases, thus far, six cases were reported from Western Canada, one from Central Canada and one from Northern Canada.

The 8 confirmed cases were 3 to 15 years of age, 7 were Aboriginal and 1 child was born overseas. Two cases were microbiologically proven, 2 were presumptively diagnosed based on the case definition criteria, and 4 were clinical diagnoses. All children had intrathoracic disease and one also had extra pulmonary disease. In the two cases that grew *Mycobacteria tuberculosis*, neither showed resistance.

Conclusion

- Of the 8 confirmed cases to date, 7 were Aboriginal, and 1 child was born overseas.
- All children had intrathoracic disease, and one also had extrapulmonary disease.

Principal investigators

Shaun K. Morris, MD, MPH, FRCPC, Clinician-Scientist, Division of Infectious Diseases, The Hospital for Sick Children, 555 University Ave., Toronto ON M5G 1X8; tel.: 416-813-6625; fax: 416-813-8404; shaun.morris@sickkids.ca

Ian Kitai, MB, BCh, FRCPC, Tuberculosis Specialist, Division of Infectious Diseases, The Hospital for Sick Children, 555 University Ave., Toronto ON M5G 1X8; tel.: 416-813-6273; fax: 416-813-5032; ian.kitai@sickkids.ca

Conversion disorder in children and youth

September 2011 to August 2013 – Final report

C Krasnik, C Grant, J Cairney, A Chapman, M Connolly, S Findlay, O Jamouille, A Kam, E Lipman, R MacNay, B Meaney

Highlights

- The minimum estimated incidence of conversion disorder (CD) was 1.7 cases per 10,000 children and youth.
- The majority of the 130 confirmed cases were female, which is consistent with the literature.
- The average age of confirmed cases was 14 years (range 8–18 years).
- Most patients had a time delay to diagnosis of between one and six months and saw multiple physicians.
- Antecedent stressors, such as bullying, parental separation, academic pressure, and a personal and/or family history of depression and/or anxiety were reported in 95% of cases.

Background and objectives

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance.

Case definition

A new patient less than 18 years of age with suspected or diagnosed conversion disorder* defined as the persistent appearance of symptoms/signs that affect the patient's:

- Voluntary motor function (e.g., weakness, abnormal gait or movements, difficulty with swallowing or loss of speech) **and/or**
- Sensory function (e.g., loss or diminished sensation of touch, sight, or hearing) **and/or**
- Non-epileptic seizures ("pseudo-seizures" or "psychogenic seizures")

and suggest a neurological or medical disease/condition

and

- May be accompanied by psychological factors at presentation
- Cause significant distress and/or impairment in daily activities, such as self-care, school, play, peer and family relationships and/or activities

and

- May be accompanied by psychological factors at presentation
- Cause significant distress and/or impairment in daily activities, such as self-care, school, play, peer and family relationships and/or activities
- and
- Cannot be adequately explained by a medical condition, substance abuse, or other mental disorder according to the clinical judgment of the treating physician after a comprehensive physical exam and appropriate investigations
- Show no evidence that they have been intentionally produced

* If the diagnosis is uncertain or awaiting confirmation, the case should still be reported.

Exclusion criteria

A patient who has predominantly or exclusively symptoms that are: secondary to substance abuse; intentionally produced; secondary to pain disorder, somatization disorder or fatigue; due exclusively to another psychiatric disorder, such as depression, psychosis or tic disorder diagnosed by a child psychiatrist

Results

National surveillance methodology through the CPSP was used to study the incidence and clinical characteristics of paediatric conversion disorder in Canada. From September 1, 2011 to August 31, 2013, a total of 195 cases were reported to the CPSP with 130 of those confirmed. The detailed questionnaire completion rate at the time of

Surveillance Studies in 2013

analysis was 76%, leaving 44 reported cases pending. Twenty-one cases were excluded either because of duplication or not meeting eligibility criteria. Of the 130 confirmed cases, 28% were male and 72% were female, with an average age of 14 years (range 8–18 years). Approximately 10% of cases were children 10 years of age or younger and only 4 of these 13 children were male. The minimal estimated incidence of conversion disorder is approximately 58 cases per year in the Canadian paediatric population.

Year	Reported	Duplicate	Excluded	Pending	Confirmed
2011*	40	1	3	11	25
2012	98	6	6	23	63
2013†	57	2	3	10	42
Total	195	9	12	44	130

* September 1 to December 31, 2011

† January 1 to August 31, 2013

Demographically, 55% of cases originated in Ontario, 25% in Western Canada, 12% in Quebec, and the remaining 8% of cases were in Atlantic Canada. Three quarters (75%) were Caucasian, 9% were Black, 7% were First Nations, with the remaining 9% being Asian, Middle Eastern or of unknown ethnicity.

The majority of cases (87%) had multiple conversion symptoms, which varied widely across the spectrum. These included altered motor function, altered sensation, altered or loss of consciousness, visual changes, speech disturbances, psychosis and dizziness. The most common presentations were disturbance of voluntary motor function (56%), abnormal movements (45%), pseudo-seizures (42%), sensory symptoms (38%), visual deficits (27%), speech disturbance (11%) and hearing deficits (7%).

Hospital admission was required to determine diagnosis in 63% of the cases, with an average stay of 13 days (range 1–110; SD \pm 20.3). On average, five specialists and subspecialists were involved in the diagnostic work-up of these youth (range 1–13; SD \pm 2.5). The specialists consulted most frequently were paediatricians followed by child psychiatrists. The most common subspecialty consulted was paediatric neurology followed by adolescent medicine. There were also multiple consults within specialties. The average number of investigations done per case was 3.5 (range 0–9; SD \pm 1.7), typically consisting of extensive blood work, brain imaging (>90% had MRI/CT scans), EEG and EMG studies. Antecedent stressors (family conflict, bullying, academic pressure, peer pressure, abuse, and a personal and/or family history of depression and/or anxiety) were reported in 95% of cases. A prior history of mental health concerns was reported in 37% of cases and 38% of cases had a family history of anxiety and/or depression. In terms of functional impairment, approximately 65% of affected adolescents had missed school for an average of 36 days (range 1–300; SD \pm 58).

Psychotropic medications for anxiety or depression had been previously prescribed in approximately 28% of cases. The average duration of symptoms, from time of onset to diagnosis, was between one and six months, with most cases (72%) confirmed by the six-month time point.

Discussion

Conversion disorder is a significant burden for affected children and adolescents, their families, and the Canadian health system, with a minimum estimated incidence of 1.7 cases per 10,000 children. CPSP results indicate a female gender preponderance and an adolescent age distribution that are consistent with the literature. The identified association of CD with anxiety and depression highlights the potential impact of more common life stressors. Identifiable stressors were found in 95% of cases, which is higher than the 60% to 70% range reported in the literature. However, the types of stressors reported are consistent with Australian and British surveillance studies.

There was a considerable time delay of between one to six months from onset to diagnosis and many patients saw several health professionals with numerous investigations performed prior to being definitively diagnosed. The delay suggests a potential lack of awareness and also a reluctance to consider conversion disorder as a positive diagnosis as opposed to a diagnosis of exclusion.

Conclusion

- The minimal estimated incidence of conversion disorder is 1.7 cases per 10,000 children.
- Female gender, adolescent age and multiple common life stressors were common among affected individuals.
- Multiple specialty physician visits and considerable time delay were common prior to diagnosis.
- Clinical guidelines for the diagnosis and management of conversion disorder may be helpful in improving patient care and minimizing health care utilization.

Publications and presentations

Krasnik C, Grant C. Conversion disorder: Not a malingering matter. *Paediatr Child Health* 2012;17(5):246

Krasnik CE, Grant C. Conversion disorders in Canadian children and youth: A national survey of clinical features and treatment outcomes. International Congress of Pediatrics, Melbourne, August 2013. (Poster presentation)

Krasnik CE, Grant C. Canadian Paediatric Surveillance Program (CPSP) conversion disorders in children and youth: Preliminary data from a national survey of clinical features and treatment outcomes. Canadian Paediatric Society Annual Conference, Edmonton, June 2013. (Oral presentation)

Grant C, Krasnik CE. Understanding conversion disorder: Does the mind rule the body or does the body rule the mind? Canadian Paediatric Society Annual Conference, Edmonton, June 2013. (Poster presentation)

Principal investigators

Catherine Krasnik, MD, PhD, FRCPC, Assistant Clinical Professor (Adjunct), Psychiatry and Behavioural Neurosciences, McMaster University, 3G48-1200 Main St W, Hamilton ON L8N 3Z5; tel.: 905-572-1838; fax: 905-308-7548; krasnice@mcmaster.ca

Christina Grant, MD, FRCPC, Associate Professor, Division of Adolescent Medicine, Department of Paediatrics, McMaster University, 3G48-1200 Main St W, Hamilton ON L8N 3Z5; tel.: 905-521-2100, ext. 75644; fax: 905-308-7548; chgrant@mcmaster.ca

Early-onset major depressive disorder

January 2012 to December 2014

D Korczak, M Feldman, J LeBlanc, M Ofner, P Parkin, S Wong

Highlights 2012 and 2013

- Fifteen cases were confirmed since the start of the early-onset major depressive disorder (EOMD) study.
- As nine cases (60%) were male, the study does not demonstrate the female predominance that characterizes adolescent depression.
- Eleven cases (73%) were impaired in three or more functional domains and 10 (67%) had been symptomatic for at least six months prior to presentation.
- Maternal history of depressive disorder was present for 10 cases (67%), and psychiatric comorbidity was present in 13 cases (87%).

Background and objectives

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance.

Case definition

A child 5 to 12 years of age inclusively, seen in the previous month, with newly diagnosed early-onset major depressive episode, including a child with unipolar mood disturbances sufficient to cause a disruption to social, family and/or academic functioning

“Major depressive episode” is defined in DSM-IV-TR as:

- 1) Depressed or irritable mood, most of the day, nearly every day,

or

- 2) Markedly diminished interest or pleasure in all, or almost all, activities most of the day,

which is either newly present or has clearly worsened compared with the child’s pre-episode status,

and

At least **four** of the following seven symptoms present during the same two-week period as either (1) **or** (2) above. These symptoms occur daily or near daily and represent a distinct change from previous functioning.

- 1) Significant weight change, failure to make expected weight gains **or** significant appetite change
- 2) Insomnia (difficulty falling asleep, night-waking or waking too early) **or** hypersomnia
- 3) Psychomotor agitation **or** retardation: observable by others and does not represent subjective feelings
- 4) Fatigue **or** loss of energy
- 5) Feelings of worthlessness **or** excessive or inappropriate guilt (not merely guilt about being sick)
- 6) Diminished ability to think or concentrate, **or** indecisiveness
- 7) Recurrent thoughts of death, recurrent suicidal ideation, **or** a suicide attempt

and

Impairment in social functioning (social withdrawal, family or peer conflicts) or academic functioning (school refusal, decreased school performance), which is either newly present or worsened compared with pre-episode status

Exclusion criteria

- 1) Symptoms due to the direct physiological effects of a substance or a general medical condition
- 2) Symptoms occurring exclusively during acute bereavement period (within two months after the loss of a loved one). Note: This exclusion does not apply to palliative care patients
- 3) A previous diagnosis of a manic episode or bipolar disorder

Results

At the end of the second year of surveillance, 30 EOMD cases were reported and 15 cases were confirmed. These numbers are lower than those anticipated based on the literature. The detailed questionnaire completion rate at the time of analysis for both years was 87%. Of the 30 cases initially reported, 10 were excluded: 9 cases due to age older than 12 years, and 1 case due to subsequent revocation of a diagnosis by a child psychiatrist. Of the 15 confirmed cases, 9 (60%) were boys. Children with early-onset depression were generally globally impaired in all functional domains.

Reported	Duplicate	Excluded	Pending	Confirmed
30	1	10	4	15

Ten of 15 children (67%) with depression reported distressing symptoms for more than six months, and five of these for more than 12 months, prior to presentation. Ten of the 15 children had a maternal history of major depressive disorder, consistent with epidemiological data reporting increased familiarity of early-onset depression and early age of onset among offspring of depressed individuals. Psychiatric comorbidity was present in 13 cases (87%), most commonly ADHD and anxiety, indicating very early onset of difficulties with affective and behavioural regulation among these children. Most cases (n=11, 73%) were receiving medication. Of these, seven were also receiving psychotherapy. Ten of the 11 cases receiving antidepressant medication were treated with a selective serotonin reuptake inhibitor (SSRI): 6 cases were treated with fluoxetine, 2 were treated with citalopram, and 1 each received escitalopram and sertraline. Six patients (40%) were treated with two or more medications.

The number of cases reported was too small to draw conclusions regarding incidence. However, these preliminary data are consistent with the literature in suggesting that early-onset depression is a familial, debilitating illness that may be present for a prolonged period of time prior to presentation. Increased knowledge regarding the incidence and presentation of children affected with EOMD is important in designing effective diagnostic and management approaches for children with this treatable illness.

Conclusion

- Most children with childhood-onset depression were globally impaired in all functional domains.
- Psychiatric comorbidity was present in nearly all cases, most commonly ADHD and anxiety.
- Children with EOMD are frequently treated with antidepressant medication, either singly or in combination with psychotherapy.

Publications and presentations

Korczak DJ. Identifying depression in childhood: Symptoms, signs and significance. *Paediatr Child Health* 2012;17(10):572

Principal investigator

Daphne Korczak, MD, FAAP, FRCPC (paediatrics), FRCPC (psychiatry), The Hospital for Sick Children, University of Toronto, Room 35A, 1145 Burton Wing, 555 University Ave, Toronto ON M5G 1X8; tel.: 416-813-6510; fax: 416-813-5326; daphne.korczak@sickkids.ca

Fragile X syndrome

April 2012 to March 2014

G Aubertin, J Down, G Graham, T Nelson, M Ofner, C Paribello

Highlights 2013

- In 2013, 14 cases of fragile X syndrome (FXS) were confirmed.
- The average age at post-natal diagnosis was 3.5 years.
- A close family history of either confirmed FXS or intellectual disability/autism was present in three cases with a delayed diagnosis (ages 5, 5 and 7 years).
- Comorbid diagnoses included speech and communication problems (71%) and autism (50%).

Background and objectives

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance.

Case definition

A new patient less than 18 years of age with diagnosed fragile X syndrome meeting the following criteria:

- 1) **Genetic criteria:** Males or females, with laboratory confirmation of a CGG-repeat allele in the full mutation size range (>200 repeats), including mosaicism

and

- 2) **Clinical criteria, one** of the following:
 - Global developmental delay, manifesting as the clinical impression of delays in two or more domains of development **or**
 - Intellectual disability, mild, moderate or severe, diagnosed through standardized psychological testing **or**
 - Asymptomatic infant, tested because of a positive family history, including prenatally diagnosed cases

Exclusion criteria

Clinical evidence of global developmental delays or intellectual disability with laboratory confirmation of a CGG-repeat allele in the normal or premutation size range

Results

In 2013, there were 21 reported cases, of which 14 have been confirmed with receipt of completed questionnaires.

The detailed questionnaire completion rate at the time of analysis was 71%. Of these confirmed cases, 13 were reported to be male and one was not specified. One case

was diagnosed prenatally based on a known family history. For the remaining cases, the average age at post-natal diagnosis was 3.5 years (range 20 months to 7 years), which is in keeping with the literature.

Reported	Duplicate	Excluded	Pending	Confirmed
21	0	1	6	14

Two of the cases had a known family history of FXS and two other cases had siblings suspected of having FXS who were awaiting testing. Three of these cases had a significantly delayed diagnosis (two at age 5 and one at age 7). In three cases, a family history of FXS was unknown; in one of these cases the child was adopted. In the remaining seven cases (50%) there was no known family history of FXS or FX-related conditions.

Speech and communication problems were the most commonly reported medical concerns, present in 10 (71%) cases. Autism was frequent, both as a referring condition (n=5, 36%) and as a reported comorbidity (n=7, 50%), but this may be underestimated since several of the children had not undergone autism evaluation at the time of reporting. Other comorbidities included recurrent otitis media (n=4, 29%), sleep apnea (n=2, 14%) and seizures (n=1, 7%). The frequency and range of associated medical concerns was consistent with the literature but may be under-reported for two reasons: many of the children were reported to the CPSP with a new diagnosis of FXS

before they had been fully evaluated for possible complications; and the results of these assessments were not always available to reporting physicians.

Half of the confirmed cases were from Ontario while the rest were from British Columbia, Alberta, Saskatchewan, Manitoba and Quebec. These numbers are in keeping with the majority of the Canadian population, but notable is the absence of cases from Atlantic Canada. A low prevalence of FXS in the Maritimes has previously been reported. The reported ethnicities included Caucasian (57%), Chinese (14%), other Asian (7%), mixed East Indian/Middle Eastern/Caucasian (7%), First Nations (7%), and Black (7%). The prevalence is assumed to be similar across ethnicities, but there have been concerns in the literature about less diagnostic testing in non-Caucasian populations. Preliminary results indicate that, in Canada, new diagnoses of FXS are not limited to the Caucasian population.

Discussion

There is limited information in the medical literature on the demographics of FXS in Canada. This ongoing study aims to ascertain the minimum incidence of new FXS diagnoses, along with data on demographics, clinical features, burden of illness and management approaches in Canada. A better understanding of the characteristics of the FXS patient population is essential, given two recent developments in the field: increasing newborn screening and novel pharmaceutical agents in clinical trials, giving rise to speculations that targeted therapies will be available to patients in the next few years. Results to date indicate that the age at diagnosis, ethnicity, geographic distribution and medical comorbidities are within the ranges expected for the newly diagnosed FXS population. The study is ongoing for another year with the goal of increasing the number of confirmed cases to a level that will allow more robust statistical analysis.

Conclusion

- Three cases in 2013 had a significantly delayed diagnosis (two at age 5 and one at age 7).
- In 50% of cases, there was no known family history of FXS or FX-related conditions.
- Preliminary results indicate that new diagnoses of FXS are not limited to the Caucasian population.

Publications and presentations

Aubertin G. Fragile X syndrome: Are paediatric health care providers missing the diagnosis? *Paediatr Child Health* 2013;18(5):251-2

Principal investigators

Gudrun Aubertin, MD, MSc, FRCPC, Clinical Geneticist, Vancouver Island Medical Genetics/University of British Columbia, Victoria General Hospital, Victoria BC V8Z 6R5; tel.: 250-727-4419; fax: 250-727-4295; gudrun.aubertin@viha.ca

Jonathan Down, MB, MHSc, FRCPC, Developmental Paediatrician, Vancouver Island Health Authority, Queen Alexandra Centre for Children's Health, 2400 Arbutus Rd, Victoria BC V8N 1V7; tel.: 250-519-6745; fax: 250-519-6931; jonathan.down@viha.ca

Kawasaki disease

November 2013 to November 2014

R Yeung, R Scuccimarri, D Cabral, N Dahdah, DG Human, HA Hume, B Lang, B McCrindle, S Schwartz

Highlights 2013

- In the first two months of surveillance, 26 cases of Kawasaki disease (KD) were confirmed.
- All but one patient received IVIG therapy; of these, two developed evidence of hemolysis.
- Study results may have important implications for disease management and patient advocacy.

Background and objectives

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance.

Case definition

A new patient presenting before the age of 18 years with a definite or presumed diagnosis of Kawasaki disease:

1) **Complete KD**, defined as fever persisting for five* days or more

AND the presence of **at least four** of the following clinical criteria:

- Changes in the peripheral extremities
 - erythema of the palms and/or soles; edema of the hands and/or feet; periungual desquamation
- Polymorphous rash
- Bilateral bulbar conjunctival injection without exudate
- Changes in the lips and oral cavity
 - erythema and/or cracking of the lips; strawberry tongue; diffuse erythema of the oropharynx
- Cervical lymphadenopathy > 1.5 cm diameter, usually unilateral

* Presumptive diagnosis and initiation of treatment may be made before the fifth day of fever.

2) **Incomplete KD**, defined as fever of five days or more and less than four clinical criteria

3) **Other KD**, defined as KD not fulfilling criteria for complete or incomplete KD but presumed because of a feature on echocardiogram or follow-up (i.e., periungual desquamation) that has led the treating physician to recommend treatment and/or cardiac follow-up

Results

In the first two months of surveillance, 51 unique cases of acute Kawasaki disease were reported, and 26 of these were confirmed. Of the 26 cases, 18 (69%) were male. The median age at diagnosis was 2.8 years (range 0.6–14.0 years). Eighteen (69%) cases had complete KD and eight (31%) had incomplete presentation. Paediatric rheumatologists members of CAPRI (Canadian Alliance of Paediatric Rheumatology Investigators) are also reporting cases to the CPSP.

Reported	Duplicate	Excluded	Pending	Confirmed
51	2	0	23	26

Eight patients were Caucasian, 6 were Asian, 2 were Black, 2 were of mixed ethnicity, 1 was reported as 'other' and the remaining ethnicities were unknown (n=7). Twenty (77%) cases were from Ontario, and the remaining six were from Quebec, Alberta, British Columbia and Saskatchewan. All but one patient received IVIG therapy during the acute phase of disease. Of the 25 children who received IVIG therapy, two developed evidence of hemolysis. Coronary outcome data are pending.

IVIG was used as first-line therapy in almost all cases. Short-term complications of therapy included two cases of hemolysis. Data on longer-term complications, including coronary outcome, are pending.

Kawasaki disease and potential treatment complications are a significant public health concern. The results of this study will provide much needed evidence to inform management guidelines and advocacy for access to better therapies.

Conclusion

- IVIG was the common therapy for confirmed cases.
- Short-term complications of therapy included two cases of hemolysis.
- Data on long-term complications, such as coronary outcome, are pending.

Principal investigators

Rae Yeung, MD, PhD, Professor of Paediatrics, Immunology and Medical Sciences, University of Toronto, Paediatric Rheumatologist and Senior Scientist, The Hospital for Sick Children, 555 University Ave., Toronto ON M5G 1X8; tel.: 416-813-8964; fax: 416-813-4989; rae.yeung@sickkids.ca

Rosie Scuccimarri, MD, Assistant Professor, Department of Paediatrics, McGill University, Paediatric Rheumatologist, Montreal Children's Hospital, C505-2300 Tupper St., Montréal QC H3H 1P3; tel.: 514-412-4268; fax: 514-412-4365; rosie.scuccimarri@muhc.mcgill.ca

Neonatal hyperbilirubinemia – severe (2011–2013) Infants 60 days or less

March 2011 to February 2013 – Final report

M Sgro, T Barozzino, DM Campbell, S Kandasamy, M Ofner, V Shah

Highlights

- The minimum incidence of severe neonatal hyperbilirubinemia (NHS) has declined since 2002–2004 following the introduction of the Canadian Paediatric Society’s neonatal hyperbilirubinemia guidelines in 2007.
- This study identified 90 NHS cases.
- Cases of severe hyperbilirubinemia were more likely to have a known cause in 2011–2013 than in 2002–2004.

Background and objectives

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance.

Case definition

An infant 60 days of age or less with unconjugated hyperbilirubinemia, who has had peak serum total bilirubin >425 µmol/L or neonatal exchange transfusion

Exclusion criteria

An infant who has had exchange transfusion for well-documented Rh isoimmunization disease or who was born at less than 35 weeks gestational age

Results

Over the two-year surveillance period, 144 cases of severe neonatal hyperbilirubinemia were reported in infants 60 days of age or less. Of these, 90 cases were confirmed, 27 were excluded for not meeting the case definition, 3 were duplicate reports, and 24 remain under review. At the time of analysis 83% of detailed questionnaires were returned. The 90 confirmed cases were predominantly from Ontario (n=41), Quebec (n=20), and British Columbia (n=13), while remaining cases (n=16) were from Alberta, Saskatchewan, Manitoba, Nova Scotia, and Nunavut.

All affected infants were born between 35 and 41 weeks gestation, with a mean gestational age of 38.3 weeks (SD ± 1.5) and mean birth weight of 3260 g (range 1690–4474; SD ± 454). There were slightly more males (57%) diagnosed with NHS than females (43%), and the majority of the infants (82%) were breast fed.

TABLE 1 – NHS cases from March 1, 2011 to February 28, 2013

Year	Reported	Duplicate	Excluded	Pending	Confirmed
2011*	60	1	12	10	37
2012	64	2	10	9	43
2013†	20	0	5	5	10
Total	144	3	27	24	90

* March 1 to December 31, 2011

† January 1 to February 28, 2013

TABLE 2 – Baseline demographics of infants diagnosed with severe neonatal hyperbilirubinemia in 2002–2004 as compared to 2011–2013

Demographics	2002–2004		2011–2013		p-value
National infant births	640,000		760,000		<0.001
Infants that meet definition	258		90		<0.001
Gestational age, wk, mean (SD)	39	(1.4)	38	(1.5)	NS
Sex, male (percent)	162	(63%)	51	(57%)	NS
Birth weight, g, mean (SD)	3360	(489)	3260	(454)	NS
Age at presentation, h, mean (SD)	112	(66)	117	(75)	NS
Breast-feeding (percent)	210	(81%)	74	(82%)	NS
Readmission (percent)	185	(72%)	66	(75%)	NS
Peak total bilirubin level, µmol/L, mean (SD)	471	(76)	484	(92)	NS
Weight loss of 10–15% (percent)	28	(11%)	10	(11%)	NS
Weight loss of >15% (percent)	11	(4%)	4	(5%)	NS

NS: Not significant

Various treatment options were utilized, the most common being phototherapy, exchange transfusion, and IVIG plus phototherapy.

Data from this study allowed for comparison with the previous 2002–2004 CPSP study (Table 2) on NHS before the introduction of the 2007 Canadian Paediatric Society's *Guidelines for detection, management and prevention of hyperbilirubinemia in term and late preterm newborn infants*. The number of reported and confirmed infants with NHS decreased from 258 cases in 2002–2004 to 90 cases in 2011–2013, with a minimum estimated incidence of 4/10,000 live births in 2002–2004 versus 1.2/10,000 in 2011–2013 ($p < 0.001$). The odds of NHS were 3.48 times lower (95% CI 2.72–4.47) in 2011–2013 relative to 2002–2004. This reduction may be related to changes in practice following the introduction of the Canadian Paediatric Society's guidelines for the management of neonatal hyperbilirubinemia. The mean reported peak bilirubin level was 484 $\mu\text{mol/L}$ (range 181–788; $\text{SD} \pm 92$) in 2011–2013, compared with 471 $\mu\text{mol/L}$ (range 156–841; $\text{SD} \pm 76$) in the previous study period; however, this difference was not statistically significant. Table 3 shows a breakdown of the etiology of NHS for those infants with a known cause. ABO incompatibility and G6PD deficiency were the most common causes of NHS in both studies. Cases of NHS were more likely to have a known cause in 2011–2013 versus 2002–2004 ($p < 0.001$).

TABLE 3 – Causes of severe neonatal hyperbilirubinemia

Diagnosis for severe hyperbilirubinemia	Frequency 2002–2004 (%)		Frequency 2011–2013 (%)	
	n	%	n	%
Infants with known cause	93	(36%)	54	(61%)*
Those with a known cause	n=93		n=55†	
ABO incompatibility	48	(52%)	33	(61%)
G6PD deficiency	20	(22%)	10	(19%)
Other antibody incompatibility	12	(13%)	5	(9%)
Hereditary spherocytosis	7	(8%)	0	(0%)
Urinary tract infection	2	(2%)	1	(2%)
Sepsis	1	(1%)	3	(6%)
Pyruvate kinase deficiency	1	(1%)	1	(2%)
Hypothyroidism	1	(1%)	0	(0%)
Unstable hemoglobin	1	(1%)	0	(0%)
Birth trauma	0	(0%)	2	(4%)

* $p < 0.001$

† One infant was diagnosed with two known causes: sepsis and urinary tract infection

Conclusion

- The odds of NHS were three times lower in 2011–2013 relative to 2002–2004 following the introduction of the 2007 CPS guidelines.
- ABO incompatibility and G6PD deficiency were the most common causes of NHS in both studies.

Publications and presentations

Sgro M, Kandasamy S, Campbell D, Shah V, Grenier D, Ofner M. Surveillance of severe neonatal hyperbilirubinemia in Canada: 2011–2013. International Congress of Pediatrics, Melbourne, August 2013. (Poster presentation)

Sgro M, Kandasamy S, Ofner M, Campbell D, Grenier D, Simone L. Comparing rates of severe neonatal hyperbilirubinemia in three western, industrialized populations: Canada, the United Kingdom and Ireland, and Switzerland. International Congress of Pediatrics, Melbourne, August 2013. (Poster presentation)

Sgro M, Kandasamy S, Campbell D, Ofner M, Shah V. Surveillance of severe neonatal hyperbilirubinemia in Canada: 2010–2013. Canadian Paediatric Society Annual Conference, Edmonton, June 2013. (Poster presentation)

Sgro M. Severe neonatal hyperbilirubinemia and bilirubin encephalopathy in Canada. Audrey K. Brown Kernicterus Symposium, PAS/ASPR Annual Conference, Boston, April 2012. (Oral presentation)

Sgro M. Incidence of chronic bilirubin encephalopathy in Canada, 2007–2008. Annual Neonatal & Maternal-Fetal Medicine Research Day, University of Toronto, Toronto, April 2012. (Oral presentation)

Principal investigator

Michael Sgro, MD, FRCPC, University of Toronto, Department of Paediatrics, Li Ka Shing Knowledge Institute, St. Michael's Hospital, Room 014, 15th floor, Cardinal Carter Wing, 30 Bond St, Toronto ON M5B 1W8; tel.: 416-864-6060, ext. 6560; fax: 416-864-6073; sgrom@smh.ca

Periodic fever syndromes

September 2011 to August 2014

P Dancey, S Bensele, M Gattorno, AK Junker, RM Laxer, P Miettunen, LA Turner

Highlights 2013

- The study confirmed 41 cases of periodic fever syndromes (PFS).
- Periodic fever aphthous stomatitis, pharyngitis and adenitis (PFAPA) was the most frequently reported diagnosis followed by unidentified PFS.
- The average number of fever attacks per year was high: 10 for PFAPA and undefined PFS cases, and 17 for familial Mediterranean fever.
- Symptom onset occurred on average two years prior to diagnosis.

Background and objectives

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance.

Case definition

A patient less than 18 years of age presenting with a newly diagnosed periodic fever syndrome (autoinflammatory syndrome) meeting the criteria outlined below

Inclusion criteria

The patient must have one of the following diagnoses (see appendix and table in protocol for specific details and characteristic features):

- Familial Mediterranean fever (FMF)
- Tumor necrosis factor receptor-associated periodic syndrome (TRAPS)
- Hyperimmunoglobulinemia D syndrome (HIDS)
- Cryopyrin-associated periodic syndromes (CAPS), including familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), and neonatal-onset multisystem inflammatory disease (NOMID)
- Periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA)
- Periodic fever syndrome – undefined

Exclusion criteria

- Detailed clinical assessment and investigations compatible with infections, malignancy, or the classical inflammatory or autoimmune rheumatic diseases (e.g., systemic lupus erythematosus, systemic juvenile idiopathic arthritis, inflammatory bowel disease)
- Febrile attacks with regular periodicity and low neutrophil counts, suggestive of cyclic neutropenia

Results

During the 2013 surveillance, 59 cases of PFS were reported. The detailed questionnaire completion rate at the time of analysis was 76%. Of the 41 confirmed cases, 23 were PFAPA, 14 were undefined PFS, 3 were FMF, and 1 was HIDS (Table 2). The mean age at diagnosis was 5.5 years (range 20 months to 10 years). The mean age of symptom onset occurred two years prior to diagnosis. The majority of reporting physicians were paediatric rheumatologists (54%) and general paediatricians (32%). Other paediatric specialties reporting included endocrinology, emergency medicine, infectious diseases, hematology, and gastroenterology. Patients had seen a variety of physicians leading to their diagnosis (average 2.9; range 1–6), most commonly a paediatrician, family physician or rheumatologist. Twenty-nine percent (29%) of cases had also been assessed by other specialties prior to diagnosis.

Reported	Duplicate	Excluded	Pending	Confirmed
59	1	3	14	41

PFAPA cases (n=23) had a mean age of 4 years (range 20 months to 9 years). There were 9 males and 14 females. Patients experienced an average of 10 fever attacks per year, with episodes lasting a mean of 3.9 days (Table 3). The most frequent fever-associated manifestations were pharyngitis (83%), cervical lymphadenopathy (70%),

stomatitis (65%), fatigue (61%), abdominal pain (35%) and headache (26%).

Undefined PFS cases (n=14) had a mean age of 5 years (range 20 months to 10 years). There were 9 males, 4 females, and 1 case not specified. Patients experienced an average of 10 fever attacks per year, with episodes lasting a mean of 3.7 days (Table 3). The most frequent fever-associated manifestations included abdominal pain (43%), headache (36%), vomiting (36%), diarrhea (21%), pharyngitis (21%) and stomatitis (21%). The majority of these 14 cases were considered either a suspected PFAPA, in which genetic test results to exclude other PFS types were pending, or the case met criteria for a periodic fever syndrome, however, the overall presentation was not felt to be consistent with a more specific type. Three patients were considered possible cases of FMF, CAPS, or HIDS, though confirmatory testing was not yet available.

TABLE 2 – PFS cases, mean age at diagnosis and symptom onset

PFS type	Number of cases	Mean age at diagnosis (range)	Mean age at symptom onset (range)
PFAPA	23	4 years (20 months to 9 years)	3 years (6 months to 7 years)
Undefined	14	5 years (20 months to 10 years)	2 years (6 months to 6 years)
FMF	3	5 years (4 to 7 years)	4 years (3 to 6 years)
HIDS	1	8 years	5.5 years

TABLE 3 – PFS fever patterns

PFS type	Number of fever attacks per year (range)	Duration of attacks (range)
PFAPA	10 (5–15)	3.9 days (1–7)
Undefined	10 (4–15)	3.7 days (1–7)
FMF	17 (12–25)	2.7 days (1–4)
HIDS	10	5.5 days

FMF cases (n=3) had a mean age of 5 years (range 4–7). One case was male and the remaining two were female. Patients experienced an average of 17 fever attacks per year, with episodes lasting a mean of 2.7 days (Table 3). The most frequent fever-associated manifestations were arthralgia (100%), abdominal pain (67%), pharyngitis (67%), fatigue (67%) and headache (67%). Additional features included thoracic pain, pleurisy and vomiting.

Twenty-seven percent (27%) of confirmed cases for 2013 had genetic testing results completed prior to diagnosis. When genetic testing was not requested, most cases were diagnosed with PFAPA, a condition for which no genetic test is available.

Discussion

Study results already show that periodic fever syndromes affect many Canadian children annually with recurrent, self-limiting inflammatory episodes of unprovoked fever. They present with a wide variety of fever-associated manifestations. Genetic testing of these children was frequently reported and is important to better define the PFS subtypes. Early recognition and confirmation of diagnosis open the possibility of effective treatments to ameliorate symptoms and prevent or reverse cumulative organ damage, such as renal amyloidosis, hearing loss or arthritis.

Conclusion

- Many Canadian children are affected with PFS each year with frequent attacks of fever.
- The onset of symptoms was often years prior to diagnosis.
- Genetic testing was frequently reported and is important to better define the PFS subtypes, opening the possibility of effective treatments.

Publications and presentations

Dancey P, Benseler S, Junker AK, Laxer RM, Miettunen P, Turner LA, Gattorno M. The challenge of periodic fevers in children. *Paediatr Child Health* 2012;17(3):123

Principal investigator

Paul Dancey, MD, FRCPC, Janeway Children’s Hospital, Memorial University, St. John’s NL A1B 3V6; tel.: 709-777-4766; fax: 709-777-4343; paul.dancey@easternhealth.ca

Respiratory syncytial virus infections in paediatric transplant patients

September 2010 to August 2013 – Final report

JL Robinson, HT Akwar, U Allen, I MacLusky

Highlights

- During three years of national surveillance, 24 children were reported who had respiratory syncytial virus (RSV) infection within two years of a transplant.
- Seventeen children had an uneventful course with seven of them not requiring hospital admission.
- Seven children were managed in intensive care units (ICU); two of these children died of RSV infection.

Background and objectives

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance.

Case definition

An inpatient or outpatient less than 18 years of age who has:

- Laboratory-confirmed RSV infection

and

- Received solid organ transplantation or hematopoietic stem-cell transplantation within the two previous years

Results

The incidence of severe RSV infections in paediatric solid organ or hematopoietic stem-cell transplant patients within two years post-transplant appears to be low. The mean onset of symptoms was 239 days post-transplant with five cases occurring in the first month. RSV infections occurred in all types of paediatric transplant patients, including 10 allogeneic hematopoietic stem-cell transplant recipients, 5 renal transplant recipients, 5 liver transplant recipients, 2 lung transplant recipients and 2 heart transplant recipients (18 males, 5 females, data not provided for 1 case). Eight (33%) infections were nosocomial.

Year	Reported	Duplicate	Excluded	Pending	Confirmed
2010*	4	0	2	1	1
2011	18	1	5	0	12
2012	8	0	0	4	4
2013†	8	0	1	0	7
Total	38	1	8	5	24

* September 1 to December 31, 2010

† January 1 to August 31, 2013

Seven of the 24 cases (29%) were successfully managed as outpatients, 10 (42%) were inpatients on a ward, while 7 (29%) were treated in ICU. Of these, two cases were in ICU prior to the onset of RSV and five were admitted to ICU due to RSV. Five of the seven cases required ventilation (duration of six days in two cases, and one was still ventilated at the time of case report). Two of these children died of RSV with onset of symptoms 10 and 34 days post-transplant. One of the two was treated with extra corporeal membrane oxygenation.

The known length of stay for six of the patients who did not have nosocomial RSV ranged from 1 to 21 days. No short-term sequelae due to RSV were reported in survivors.

A validation study is currently being carried out across Canada to establish the number of hospitalized eligible cases who may not have been reported to the CPSP study, and to analyze the characteristics of such patients.

Conclusion

- The incidence of severe RSV infections in paediatric transplant patients within two years post-transplant appears to be low.
- RSV infection was a cause of mortality in two patients within two years of transplant.
- Nosocomial RSV infection is a problem in transplant recipients.
- RSV prophylaxis is important, with improved infection control in hospitalized transplant recipients being vital. Ongoing surveillance of RSV infections in transplant patients remains important for establishing the costs and benefits of using palivizumab in this population.

Publications and presentations

Robinson JL, Grenier D. What happens when you mix a transplant with respiratory syncytial virus? *Paediatr Child Health* 2011;16(1):12

Robinson J, Allen U, Grenier D. Interim results for the Canadian paediatric surveillance project – Respiratory syncytial virus infections in paediatric transplant recipients. Canadian Paediatric Society Annual Conference, Edmonton, June 2013. (Poster presentation)

Principal investigator

Joan L. Robinson, MD, FRCPC, Stollery Children's Hospital, Division of Pediatric Infectious Diseases, Department of Paediatrics, University of Alberta, Edmonton AB T6G 2J3; tel.: 780-407-1680; fax: 780-407-7136; jr3@ualberta.ca

Severe alcohol intoxication in adolescents

March 2013 to February 2015

A Acker, K Thomas, D Allain, K Dow, C Korenblum, K Leslie, M Norris, A Vandermorris

Highlights 2013

- In the first year of this two-year surveillance study, 14 cases of severe alcohol intoxication (SAI) in young Canadian adolescents were confirmed.
- The mean age of presentation was 14.5 years, and there were no differences in the prevalence or presentations between males and females.
- Average blood alcohol levels were high (mean 2.58 g/L) and five adolescents required mechanical ventilation.
- Higher blood alcohol levels were more common among adolescents who had not previously consumed alcohol.

Background and objectives

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance.

Case definition

An adolescent who meets the following criteria:

- Between 11 and 15 years of age, inclusively
- Blood alcohol level >0 g/L (if available)
- Presenting with severe intoxication with impaired consciousness requiring prolonged ER observation (≥6 hours) or hospital admission

Results

In the first year of this two-year surveillance study, there were 28 reported cases. The detailed questionnaire completion rate at the time of analysis was 71%. Of these, 14 cases met the case definition. There were seven males and seven females, with a mean age of 14.5 years.

Reported	Duplicate	Excluded	Pending	Confirmed
28	1	5	8	14

Cases were reported from across the country, although no cases were reported from Prince Edward Island, New Brunswick, Manitoba or the Territories. The age of first-ever alcohol use was unknown for the majority of cases (n=11, 79%), and only 7% of these adolescents were known to have a prior emergency room visit related to alcohol use. The mean blood alcohol level for all cases was 2.58 g/L. Those adolescents who had never previously consumed alcohol tended to have higher blood alcohol levels at the time of this presentation (3.13 g/L versus 1.8 g/L). There did not appear to be a difference in blood alcohol levels between sexes; the mean blood alcohol level for male cases was 2.72 g/L versus 2.37 g/L for females (range: males 1.66–3.87 g/L, females 0.97–4.19 g/L). The majority of adolescent cases reported consuming spirits: 12 cases contained information on type of alcohol use, with 11 indicating the use of spirits. Alcohol was frequently consumed at parties (i.e., outside of the parents' home) (n=6, 43%). Concurrent use of other substances was common (n=8, 57%), most frequently cannabis. Seven of the confirmed cases that had a documented length of stay on the questionnaire were either observed in the emergency department or admitted to hospital for over 12 hours. Five of these adolescents required mechanical respiratory assistance. No child was reported to have died from severe alcohol intoxication. Follow-up was provided for 10 (71%) cases, the majority from adolescent medicine subspecialty clinics.

Compared with the number of cases reported in a similar study by the Dutch Pediatric Surveillance System examining severe intoxication in Dutch adolescents (Eur J Pediatr 2011;170(8):1023–30), these results suggest a lower incidence of severe alcohol intoxication in Canadian adolescents aged 11–15. One explanation could be an under-reporting of cases. The Dutch surveillance study reported an increase in cases reported in the second year of surveillance as information about the study became more widely disseminated. Severe alcohol intoxication

is preventable and can have significant medical and social complications. Surveillance regarding the extent of the problem among Canadian adolescents is important for promoting awareness and education for adolescents, parents, physicians and legislators.

Conclusion

- A number of Canadian adolescents between the ages of 11 and 15 with SAI presented to emergency departments or were admitted to hospitals with very high blood alcohol levels.
- Five of the confirmed cases required mechanical ventilation.
- Adolescents who had not previously consumed alcohol appeared particularly at risk, suggesting the need for increased awareness and education about the risk of alcohol intoxication among adolescents.

Publications and presentations

Acker A, Thomas K. Having some drinks: A normal part of growing up or a signal of a larger problem? Paediatr Child Health 2013;18(10):512

Principal investigators

Amy Acker, MD, FRCPC, Queen's University, Hotel Dieu Hospital, 166 Brock St., Kingston ON K7L 5G2; tel.: 613-544-3400, ext. 3362; fax: 613-544-3559; ackera@hdh.kari.net

Karen Thomas, MD, Queen's University, Department of Paediatrics, Kingston General Hospital, 76 Stuart St., Kingston ON K7L 2V7; tel.: 613-544-3400, ext. 3305; fax: 613-544-3559; thomas.k@queensu.ca

Unexpected sudden infant death and severe apparent life-threatening events in the early postnatal period

January 2013 to December 2013 – Final report

K Feldman, RK Whyte, A Howlett, G Moore, C Woolcott

Highlights

- During the surveillance period, four cases of unexpected sudden infant death (SID) and severe apparent life-threatening events (S-ALTE) in the early postnatal period were confirmed.
- The number of reported cases is lower than expected, possibly due to under-recognition, under-reporting, method of case ascertainment, strictness of the case definition, or rarity of the event.

Background and objectives

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance.

Case definition

An infant meeting **all** of the following criteria:

- ≥ 35 weeks' gestation
- Apgar score ≥ 8 at five minutes (if known)
- Acute and unexpected cardiorespiratory arrest within the first seven days of life (where day 1 is the day of birth)
- Died *or* received hospitalized mechanical respiratory support for ≥ 12 hours

Results

During one year of surveillance, 13 cases of unexpected SID/S-ALTE within the first seven days of life were reported. Of these, 4 cases were confirmed, 8 were excluded for not meeting the case definition (4 collapsed after 7 days, 2 did not die or receive respiratory support for ≥ 12 hours, and 2 cases did not occur during the surveillance period), and 1 detailed questionnaire has not been returned. The completion rate for the detailed questionnaires was 92%. Given that there are approximately 360,000 term births per year in Canada, the estimated incidence of SID/S-ALTE based on our findings is 1.1/100,000. However, this should be interpreted with caution given the low number of events reported.

Reported	Duplicate	Excluded	Pending	Confirmed
13	0	8	1	4

Case 1: A male infant was born to a 31-year-old primigravida at 37 weeks following an uncomplicated pregnancy. Delivery was vacuum-assisted for fetal bradycardia. The mother received 10 mg of morphine six hours prior to the delivery. No resuscitation was required, and Apgar scores were 9 and 9 at one and five minutes, respectively. Birth weight was 3 kg. At 1.25 hours of age, the baby was asleep while being held on his father's chest/abdomen in the delivery suite when the nurse found him limp, dusky and without a heart rate. He had last been noted to be well 25 minutes prior. Resuscitation included positive pressure ventilation, intubation, and chest compressions. His heart rate was greater than 100 bpm after two minutes. He was transferred to the NICU where he remained on a ventilator for 39 hours. He was treated with therapeutic hypothermia for 72 hours. Multiorgan involvement included apnea, hypotension requiring inotropic support for 67 hours, decreased urine output, hypoxic ischemic encephalopathy (Sarnat grade 2) and seizures. No cause for the collapse was identified. He improved and had a normal examination upon discharge at 8 days of age.

Case 2: A male infant was born at 39 weeks by Caesarean section with no preceding labour, to a 23-year-old primigravida. The mother had a relatively recent diagnosis of multiple sclerosis and was treated with amitriptyline during the first trimester. At three months gestation, the mother was obese with a body mass index of 44 kg/m². Apgar scores were 9 and 9 at one and five minutes. Birth weight was 3 kg. At approximately 46 hours of age, the mother sat the baby up after feeding and noted that he was not breathing. He had last been noted to be well by the nurse approximately five hours prior. Resuscitation included positive pressure ventilation, intubation, chest

compressions, and epinephrine. His heart rate was greater than 100 bpm after 17 minutes. He was transferred to the NICU. He remained on a ventilator for 84 hours. He was treated with therapeutic hypothermia for “neuroprotection”. Multiorgan involvement included central apnea, hypotension requiring inotropic support for 8 hours and hypoxic ischemic encephalopathy (Sarnat grade 3). No cause for the collapse was identified. The baby died at 5.5 days of age. Autopsy showed evidence of myocardial infarction and hypoxic ischemic encephalopathy. No anatomic cause of death was identified.

Case 3: A female infant was born at 41 weeks by assisted vaginal delivery due to fetal bradycardia, to a 21-year-old mother who had one previous pregnancy. The mother received limited prenatal care. There was no illicit drug use during the pregnancy, but smoking and alcohol use were unknown. No resuscitation was required, and Apgar scores were 7 and 9 at one and five minutes. Birth weight was 3 kg. The baby had an imperforate anus and rectovaginal fistula and was transferred to a tertiary care centre. At approximately 38.5 hours of age, the baby had a bradycardia spell which responded to stimulation. Approximately 1.5 hours later, the nurse was taking the baby out of the isolette for the mother to hold when the baby was noted to be dusky. Progressive bradycardia led to a cardiac arrest. Resuscitation included positive pressure ventilation, intubation, chest compressions, and epinephrine. Her heart rate was greater than 100 bpm after 50 minutes. She was treated with therapeutic hypothermia for 72 hours and remained on a ventilator for 123 hours. Multiorgan involvement included a pneumothorax necessitating chest tube insertion, hypotension requiring inotropic support for 57 hours, hypoxic ischemic encephalopathy (Sarnat grade 2) and seizures. No cause for the collapse was identified. Upon discharge at approximately 1 month of age, she was hypertonic and being treated with anticonvulsants.

Case 4: A male infant was born at 37 weeks by induced vaginal delivery to a 28-year-old mother who had three previous pregnancies. The mother had cholestasis and gestational diabetes requiring insulin during the pregnancy. No resuscitation was required, and Apgar scores were 9 and 9 at one and five minutes. Birth weight was 3 kg. At approximately 35 hours of age, the mother noted “odd breath sounds” from the baby, who was lying in his own cot. She brought the baby out to the nurse who initiated a resuscitation code as breathing and heart rate were absent. Resuscitation included positive pressure ventilation, intubation, and chest compressions. His heart rate was greater than 100 bpm after 10 minutes. Time to first respirations was 15 minutes. He was transferred to the NICU. He was treated with therapeutic hypothermia for 72 hours. He remained on a ventilator for 104 hours. Multiorgan involvement included a pneumothorax, hypoxia, hypotension requiring inotropic support for 13 hours, hypoxic ischemic encephalopathy (Sarnat grade 2) and seizures. No cause for the collapse was identified. He progressively improved and had a normal examination upon discharge to another hospital at 10 days of age.

Discussion

Significant risk factors for SID/S-ALTE which have been identified include primiparity and potentially asphyxiating position (i.e., lying prone on the breast or abdomen of the mother or close to her in a side position). Only two of the mothers in this study were primiparous, although a third mother had had a previous pregnancy but no living children. In only one case was the baby being held in a potentially asphyxiating position; maternal body mass index, a potential related factor, was not reported in this case. Other associations that have been suggested include maternal sedation/postnatal fatigue and parents being left alone with their baby. Only one mother in this study had received morphine approximately seven hours prior to her baby’s collapse. An attempt to assess the strenuousness of delivery by evaluating the length of the second stage of labour may be inaccurate due to the fact that the latter depends on parity. The length of the second stage of labour was not reported for the two primiparous women; it was approximately half an hour or less in the other two women. In only one case was a nurse present when the infant collapsed. Similar to other cases reported in the literature, no underlying causes were identified for these events.

A previous study conducted by the research team outside of the CPSP reported two cases of apparent suffocation in newborns on the maternity ward when mothers unintentionally fell asleep while breastfeeding in the side-lying position. In view of only four confirmed cases, this study could not confirm the hypothesis of side-lying or skin-to-skin practices leading to these kinds of disastrous events.

Surveillance Studies in 2013

This surveillance study resulted in a lower number of SID/S-ALTE cases than was expected (nine cases within the first 24 hours of life in term newborns). One reason may be that the case definition in this study was more stringent, requiring the baby to have died or to have received respiratory support for at least 12 hours versus only requiring bagging, intubation, and/or chest compressions. Another reason for the low number of cases could be under-reporting, either from a failure to recognize cases or a reluctance to report them. Fear of medico-legal implications or the time required to complete the detailed questionnaire may also have been factors. Finally, it is possible that the low number of early postnatal SID/S-ALTE cases identified could indicate that such events are rare.

Conclusion

- Over a one-year period, four cases of early postnatal SID/S-ALTE were confirmed with no underlying causes identified.
- The incidence of early postnatal SID/S-ALTE in Canada may be low or under-reported.
- Further research is needed to identify associated risk factors.

Publications and presentations

Feldman K. The unexpected: Sudden infant death in the postnatal period. *Paediatr Child Health* 2013;18(7):360

Principal investigators

Kayla Feldman, MD, FRCPC, Department of Paediatrics, North York General Hospital, 4001 Leslie St., Toronto, ON M2K 1E1;
kayla.feldman@gmail.com

Robin K. Whyte, MB, FRCPC, IWK Health Centre, Division of Neonatal-Perinatal Medicine, Dalhousie University, 5850/5980 University Ave.,
PO Box 9700, Halifax NS B3K 6R8; tel.: 902-470-7426; fax: 902-470-6469; robin.whyte@dal.ca

Survey Questions

Asymptomatic adrenal suppression – Post-study survey

April 2013

A Ahmet, E Goldbloom

Children with adrenal suppression (AS) may be asymptomatic, have non-specific signs and symptoms or be critically ill (adrenal crisis). Identifying and treating asymptomatic patients *before* they develop symptoms may reduce morbidity in this population. Official guidelines for screening for AS have yet to be developed. Consequently, screening practices – as demonstrated in the pre-study survey – are highly variable.

Before and after a two-year CPSP surveillance study of *symptomatic* AS, participants were surveyed to assess their screening practices for, and recognition of, AS. Results of the one-time pre-study survey were published in the *CPSP 2010 Results*. The post-study survey aimed to evaluate current practices of participants and assess the educational impact of the two-year study. The one-time post-study survey was sent to 2465 CPSP participants in April 2013. The response rate was 21% (n=521), compared to 32% in the pre-study survey. The percentage of physicians who reported routinely screening patients on GCs for AS increased from 10% in the pre-study survey to 21%. The number of physicians who reported having a screening policy in their office/centre also increased (from 6% to 11%). These increases may be attributable to awareness generated by the surveillance study. However, there was little change in the percentage of physicians who had diagnosed a child/youth with asymptomatic AS in the preceding year (from 12% to 10%).

First morning cortisol was the most frequently used test in both the pre- and post-study surveys (74% and 82% respectively). However, the low-dose ACTH stimulation test was used more often in the post-study survey – 21% in the pre-study survey compared to 43% in the post-study survey – suggesting an improved understanding of how to diagnose AS. One hundred and forty-four (28%) respondents reported that they had changed their approach to managing patients on GCs for AS over the past two years. Changes included closer surveillance of growth (n=117), routine screening (n=52), change in office policy (n=12), and change in hospital policy (n=7). Sixty-seven (13%) of the total respondents reported that their screening practice for AS changed because of the CPSP study – 65 changed their practice for inhaled corticosteroids (ICS) and 43 for systemic GCs.

Results of the previous two-year surveillance study suggested that children treated on the high but common dose of 500 mcg/day of fluticasone or greater should be screened for AS. In the post-study survey, 484 respondents answered a question regarding screening threshold for ICS; 223 (46%) do not screen children receiving only ICS, 153 (32%) screen for doses \geq 500 mcg/day of fluticasone (or equivalent), 71 (15%) screen for doses $>$ 500 mcg/day and 37 (8%) reported “other”. A similar question in the one-time pre-study survey demonstrated that among the physicians who were screening patients taking ICS, $>$ 500 mcg/day was the most common threshold (n=47), followed by \geq 500 mcg/day (n=32). The shift to the lower threshold over time (i.e., \geq 500 mcg/day vs. $>$ 500 mcg/day) suggests improved awareness of the risks of AS.

Although screening for asymptomatic AS appears to have increased following the two-year study, the frequency of screening remains low compared with the frequency of children being treated with GCs. Development of a clinical practice guideline could increase awareness of asymptomatic AS among Canadian paediatricians and increase the identification of asymptomatic AS, before symptoms develop.

Principal investigators

Alexandra Ahmet, MD, FRCPC, Division of Endocrinology and Metabolism, Children’s Hospital of Eastern Ontario, Ottawa ON K1H 8L1; tel.: 613-737-7600, ext. 3357; fax: 613-738-4236; aahmet@cheo.on.ca

Ellen Goldbloom, MD, FRCPC, Division of Endocrinology and Metabolism, Children’s Hospital of Eastern Ontario, Ottawa ON K1H 8L1; tel.: 613-737-7600, ext. 2842; fax: 613-738-4236; egoldbloom@cheo.on.ca

Managing patients with adverse events following immunizations or contraindications to vaccination

March 2013

KA Top, G De Serres, SA Halperin, J Zafack, for the PCIRN (PHAC/CIHR Influenza Research Network) investigators

Vaccination is one of the most effective public health interventions ever developed, having led to dramatic reductions in childhood morbidity and mortality. Although vaccines are generally safe, they have been associated with rare moderate or severe adverse events (e.g., febrile seizure, anaphylaxis). Patients with adverse events following immunization (AEFI) occasionally come to medical attention, and in such cases, physicians and patients may have concerns about the safety of proceeding with further immunizations. These patients can benefit from a detailed assessment by an expert clinician, as do those with underlying medical conditions that may alter the risk of an adverse event. In Canada, the Special Immunization Clinics (SIC) network was established in 2013 at 13 centres across Canada to provide expertise in the clinical care of patients with AEFI and potential contraindications to immunization.

A one-time survey was conducted to describe the current referral patterns for children with AEFI or potential vaccine contraindications among paediatricians and subspecialists in Canada and to assess paediatricians' willingness to refer such patients to a SIC, in anticipation of establishing the SIC network. The survey was distributed to 2490 paediatricians and paediatric subspecialists through the CPSP with a response rate of 24%. A majority of respondents (53%) practised general paediatrics exclusively, 4% practised infectious diseases (ID) or allergy subspecialties, 25% practised general paediatrics and a subspecialty other than ID or allergy, and 16% practised another subspecialty only. In total, 52% of respondents reported that they administer vaccines.

In the past 12 months, 29% of respondents had received questions or referrals for children with challenging AEFI or potential vaccine contraindications, including 84% of ID and allergy specialists. Family physicians were the most frequent source of referrals, followed by general paediatricians and public health professionals. Twenty-six percent (26%) of respondents had referred a patient with AEFI to another specialist in the past 12 months, most commonly an allergist or infectious disease specialist.

Few respondents expressed dissatisfaction with available resources for managing patients with AEFI (2% very dissatisfied, 7% somewhat dissatisfied), compared to the proportion that was satisfied (24% very satisfied, 24% somewhat satisfied), but there was a high frequency of non-response (44%). Overall, 69% of respondents indicated that they would be likely or very likely to refer patients to a SIC, and 34% indicated that they would have referred at least one patient to a SIC in the previous 12 months.

In conclusion, patients with challenging AEFI or potential vaccine contraindications are encountered by paediatricians and subspecialists in a variety of practice settings, and there appears to be broad support for a SIC network among Canadian paediatricians. With 13 sites in six provinces, the SIC network will be well positioned to support paediatricians and subspecialists in managing these patients. An article entitled, "Canadian paediatricians' approaches to managing patients with adverse events following immunization: The role for a special immunization clinic" was submitted to *Paediatrics & Child Health* and accepted for publication in 2014.

References are available upon request.

Principal investigator

Karina A. Top, MD, MSc, Assistant Professor of Pediatrics and Community Health & Epidemiology, Dalhousie University and Canadian Center for Vaccinology, IWK Health Centre, Halifax NS B3K 6R8; tel.: 902-470-6343; fax: 902-470-7232; karina.top@dal.ca

Paediatric palliative care

September 2013

C Cyr

Paediatric palliative care focuses on achieving the best possible quality of life for children with life-threatening conditions and their families. To achieve this goal, paediatricians have to identify the needs of children with life-threatening conditions and provide care that responds adequately to suffering. This survey investigated how paediatricians define paediatric palliative care and their perception of the needs of children with life-limiting diseases.

A one-time survey was sent to 2485 Canadian paediatricians and subspecialists. Of a total of 416 respondents (17% response rate), 219 (53%) cared for a patient with palliative care needs during the month before receiving the survey. Most paediatricians (78%) defined palliative care as end-of-life care and more, 17% defined it as end of life only, and 5% did not include a definition. A majority (58%) agreed with the four broad groups of children who would benefit from paediatric palliative care (progressive conditions in which treatment is exclusively palliative after diagnosis, conditions for which curative treatment is possible but may fail, conditions requiring intensive long-term treatment aimed at maintaining quality of life, and conditions involving severe, non-progressive disability, causing extreme vulnerability to health complications).

Of a total of 1127 cases with palliative care needs, paediatricians cared directly for 861 cases (76%) without referral to a palliative care team. Most frequently identified palliative care needs were support for family members (94%), coordination of services in the community (88%), physical symptom management (84%), respite care (81%), support for the patient (80%) and care at the time of death (78%). Only 48% felt that their patients were receiving all the services needed. Paediatricians cited the need for many types of palliative care services, such as more support to manage their palliative patients with multidisciplinary teams (19%), more education about palliative care (14%) and easier access to palliative expertise or a palliative care team (13%). Overall, only 35% had referred their patients to a palliative care team and 18% did not have access to a multidisciplinary team.

Canadian paediatricians care for a large number of children with palliative care needs. Despite recommendations to refer children to palliative care early in the course of illness, many paediatricians define palliative care as similar to hospice care. This survey suggests that Canadian paediatricians need to become familiar and comfortable with the provision of palliative care to children. Enhanced exposure to palliative care during residency training and continuing education programs would be beneficial and could include topics such as palliative medicine, grief and loss, managing prognostic uncertainty, decisions to forgo life-sustaining medical treatment, and spiritual dimensions of life and illness.

Principal investigator

Claude Cyr, MD, Centre hospitalier universitaire de Sherbrooke, Site Fleurimont, Sherbrooke QC J1H 5N4; tel.: 819-346-1110, ext. 74634; fax: 819-564-5398; Claude.Cyr@USherbrooke.ca

International Developments

The International Network of Paediatric Surveillance Units (INoPSU) provides a highly successful and easily accessible platform for international research. No other network enables international comparisons of demographics, diagnosis, treatments and outcomes for rare childhood conditions.

Established in 1992, INoPSU now includes 12 paediatric surveillance units (PSUs) among its membership. Incredibly, many of the units have been collecting data on rare childhood conditions for 20 years or more. Over 300 rare conditions have been studied to date, including rare infectious and vaccine-preventable diseases, mental health disorders, child injuries and immunological conditions. The network encompasses approximately 10,000 child health care providers who voluntarily contribute data on these rare diseases every month. Congratulations to PSUs across the globe that have contributed to the success of INoPSU over the last 15 years.



An annual report highlighting INoPSU's success was published in 2013 and can be accessed at www.inopsu.com. The network also launched its new website in 2013, which features links to the individual PSUs, lists of current and concluded studies, publications and much more. A new logo was also introduced to help promote the important work of the network.

The Australian Paediatric Surveillance Unit (APSU) celebrated its 20-year anniversary and published *Australian Paediatric Surveillance Unit: 20 Years of Research into Rare Diseases* to showcase its success over the past two decades. The publication can be accessed on the APSU website at www.apsu.org.au.

In August 2013, INoPSU's co-chairs Drs. Yvonne Zurynski (APSU) and Danielle Grenier (CPSP) welcomed members and many others to INoPSU presentations during the International Pediatric Association (IPA) Congress in Melbourne, Australia.

IPA's International Congress of Pediatrics and INoPSU meeting, Melbourne, Australia – August 2013

A session chaired by Dr. Danielle Grenier (CPSP), dedicated specifically to rare diseases, took place during the Congress and included the following presentations from Drs. Chris Verity (British Paediatric Surveillance Unit [BPSU]), Yvonne Zurynski (APSU), Odile Kremp (Orphanet, France) and Elizabeth Elliott (APSU):

- Neurological deterioration in children: What we've learnt from 20 years of surveys
- It's not easy living with a rare disease: Impacts on children and families
- ORPHANET supporting rare disease research: An international perspective
- Celebrating 20 years of the Australian Paediatric Surveillance Unit: Paediatricians' contribution to advance in practice and policy

INoPSU also had the opportunity to hold a pre-conference workshop entitled "The Power of International Collaboration to Study Rare Diseases: International Network of Paediatric



Chris Verity, BPSU and Elizabeth Elliott, APSU



Yvonne Zurynski, APSU and Allan Colver, Past Chair, BPSU

International Developments

Surveillance Units". During the workshop, members showcased their achievements over the past 15 years, highlighting the impacts of study results on clinical practice and policies. Delegates attending the workshop represented 10 different countries.

The following sessions were presented:

- Public health impacts of INoPSU data – international perspectives
- Haemolytic uraemic syndrome: international comparisons in epidemiology
- Need for data and registries for rare diseases – latest developments in Europe
- Early onset eating disorders – international comparisons in children aged <13 years
- Preventing serious injuries in children – using evidence to change policy
- Progressive intellectual and neurological deterioration in children: a complex mixture of rare conditions
- Hyperbilirubinaemia – international perspectives
- NZPSU – impacts on clinical practice and policy in New Zealand

The next IPA conference will be held in Vancouver in 2016. It will provide an opportunity to host another INoPSU scientific symposium, present various international study results to demonstrate their impact on medical and public health, and hold an INoPSU business meeting for all members.



Danielle Grenier and Marie Adèle Davis, CPSP

RESEARCH OPPORTUNITIES

Call for New Studies

Wanted

Investigators to initiate new CPSP studies

The program

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

Track record

- 80% response from approximately 2500 paediatricians
- 84% data completion rate for identified cases

Study ideas

- Adverse neonatal outcomes of delivery or labour in water
- Bronchiectasis – non-cystic fibrosis
- Congenital syphilis
- End-stage renal disease in early infancy
- Juvenile-onset recurrent respiratory papillomatosis
- Late-diagnosed cyanotic congenital heart disease
- Marijuana-induced psychosis
- Pet-related *Salmonella* infections
- Pre-school obesity with complications
- Severe neonatal hypernatremia
- Severe sports-related head trauma
- Toxic shock syndrome

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 more than 15 years, the CPSP has been an important collaborative asset for research, health policy development and the active surveillance of less common paediatric disorders. The hundreds of Canadian paediatricians and paediatric subspecialists who participate monthly in the program ensure that the CPSP is an effective way to foster continuing medical education on a wide spectrum of clinical conditions that might otherwise go largely unrecognized."

Bryce Larke, MD, Professor of Pediatrics, University of Alberta, Edmonton, Alberta, 1975–2001; Chief Medical Officer of Health, Whitehorse, Yukon, 2001–2008; CPSP Steering Committee member, 2004–2010



**For more information on the
Canadian Paediatric Surveillance Program
or a French version of this report,
please contact:**

Canadian Paediatric Society

Melanie Laffin Thibodeau, Manager, Surveillance
2305 St. Laurent Blvd.
Ottawa ON K1G 4J8
Tel.: 613-526-9397, ext. 239
Fax: 613-526-3332
cpsp@cps.ca
www.cpsp.cps.ca

Canada Post Publications Agreement number 40006512

