# Canadian Paediatric Surveillance Program: Two years of a system for investigating unusual paediatric disorders

PN Sockett PhD
*Division of Disease Surveillance, Bureau of Infectious Diseases, Laboratory Centre for Disease Control, Ottawa, Ontario*

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The Canadian Paediatric Surveillance Program (CPSP) is an active surveillance program for rare and unusual paediatric conditions of public health importance in Canada. The program was initiated in 1996 as a joint venture of the Canadian Paediatric Society (CPS) and the Laboratory Centre for Disease Control (LCDC), and is currently overseen by a steering committee representing the fields of paediatrics, epidemiology, genetics and public health. In the first two years of activity seven conditions were reported to the program via a monthly report card mailed to all clinically active paediatricians in Canada. Respondents were asked to indicate on the card the number of new cases seen for each condition and to ensure that all nil reports were also returned. Case reports were followed up with detailed report forms requesting case specific information which, when returned to the CPS, were forwarded to the principal investigator for assessment and analysis. Studies are for a minimum of one year, and new conditions may be included in the program following review by the steering committee and confirmation of ethical approval. Future development of the program includes linkage with a growing international network of paediatric surveillance units and the potential for collaboration in international studies of conditions of common interest.

**Key Words:** *Children, Epidemiology, Public health, Surveillance*

## Le programme canadien de surveillance pédiatrique : Les deux ans d'un système permettant d'analyser des maladies pédiatriques inhabituelles

Le programme canadien de surveillance pédiatrique (PCSP) est un programme de surveillance active des maladies rares et inhabituelles d'importance pour la santé publique au Canada. Le programme a été lancé en 1996 sous forme de coentreprise de la Société canadienne de pédiatrie (SCP) et du Laboratoire de lutte contre les maladies (LLCM) et est coordonné par un comité directeur composé de personnes provenant des domaines de la pédiatrie, de l'épidémiologie, de la génétique et de la santé publique. Au cours des deux premières années d'activités, sept maladies ont été déclarées au programme par l'entremise de fiches de rapport postées à tous les pédiatres cliniciens actifs au Canada. Les répondants devaient indiquer sur la fiche le nombre de nouveaux cas observés pour chaque maladie et s'assurer de déclarer aussi l'absence de nouveaux cas. Les rapports de cas étaient suivis de formulaires de rapport détaillés demandant des renseignements propres au cas qui, une fois remis à la SCP, étaient transmis à l'investigateur principal pour des besoins d'évaluation et d'analyse. Les études sont d'une durée minimale d'un an, et de nouvelles maladies peuvent être ajoutées au programme, sous réserve de l'examen par le comité directeur et de l'approbation déontologique. Parmi les futurs développements du programme, on remarque une liaison avec un réseau international croissant d'unités de surveillance pédiatrique et une participation éventuelle à l'étude internationale de maladies d'intérêt commun.

The number of uncommon diseases, conditions and infections that can affect children runs into the thousands. Individually, the number of cases is small, although many are of public health importance, and collectively they are an important cause of morbidity and mortality in childhood. By their nature, unusual or rare diseases are difficult to recognize and diagnose, and their study is hindered by the problem of obtaining sufficient data to produce meaningful results. The Canadian Paediatric Surveillance Program (CPSP) was initiated in 1996 to facilitate the surveillance and investigation of unusual or rare conditions through an active reporting program (1).

*Correspondence and reprints: Dr PN Sockett, Division of Disease Surveillance, Bureau of Infectious Diseases, PL 0603E1, Laboratory Centre for Disease Control, 3rd Floor, LCDC Building, Tunney's Pasture, Ottawa, Ontario K1A 0L2. Telephone 613-941-1288, fax 613-998-6413, e-mail paul_sockett@hc-sc.gc.ca*

The CPSP was initiated jointly by the Canadian Paediatric Society (CPS) and the Laboratory Centre for Disease Control (LCDC) of Health Canada in 1996. In the first two years of activity, the CPSP has received considerable support at both the government and program levels, as well as from the paediatric community in Canada. The program was based on the British Paediatric Surveillance Program (BPSU), which commenced reporting in 1986, and has provided a model for similar national paediatric surveillance programs in Europe, Asia and Australia (2). The benefits of the BPSU model are its ability to facilitate studies, which have resulted in increased knowledge of many disorders, to contribute to prevention or control policy development at the national level, to increase awareness among physicians and to respond to public health emergencies (2).

## AIMS AND OBJECTIVES

The CPSP was developed with a dual purpose: to serve the needs of Canadian children and youth, and to serve the research needs of professionals whose prime concern is the health and care of children. The key elements of the program are encapsulated in its mission statement: "To contribute to the improvement of the health of children and youth in Canada by national surveillance and research into uncommon paediatric diseases and conditions".

This aim is further amplified by the program's objectives.

- To develop, establish and maintain a surveillance system to monitor health in Canadian children and youth
- To involve paediatricians and professionals in related disciplines in the surveillance of rare childhood conditions of public health importance and to facilitate research into uncommon childhood disorders for the advancement of knowledge and the improvement of treatment, prevention and health care planning
- To encourage awareness and education within the medical profession of less common disorders
- To respond rapidly to public health emergencies where these relate to Canadian children and youth, by adapting surveillance activities

## MANAGEMENT

The program is managed on a day to day basis by a full-time coordinator based at the CPS in Ottawa. Additional support, when needed, is provided by the CPS (chief administrative officer) and LCDC. A small working group comprising of the CPSP coordinator, the CPS chief administrative officer and representatives from the Division of Disease Surveillance, LCDC meet as required to review the program activities and address issues that may arise.

A steering committee, formed to guide the development of the surveillance program and address key challenges for the future, determines the overall direction of the CPSP. The committee comprises experts representing the fields of paediatrics, epidemiology and related disciplines including genetics. Groups specifically represented include the CPS, LCDC, the Advisory Committee on Epidemiology, the Chief Medical Officers of Health, the Assembly of Canadian University Paediatric Department Heads and the British Paediatric Surveillance Unit. Invited observers currently include the Medical Services Branch, Health Canada, representing First Nations peoples and a liaison representative from the Canadian College of Medical Geneticists.

The steering committee meets annually in the spring to review the progress of existing studies, to consider protocols submitted for future inclusion in the CPSP and to oversee the development of the program.

**TABLE 1: Criteria for inclusion of studies in Canadian Paediatric Surveillance Program**

| | |
|---|---|
| Rarity | Disorders must be of such low incidence or prevalence that national ascertainment of cases is needed (fewer than 1000 cases a year) |
| Public health importance | Proposal must clearly address a public health issue |
| Scientific importance | Proposal must be of demonstrated scientific interest and importance |
| Uniqueness | Proposal must demonstrate a clear need for data for a condition or disorder for which there is only limited information |
| Quality of proposal | Proposal must state clear and achievable objectives, practicability, patient confidentiality, adequate resourcing, clear questionnaire and method of evaluation |
| Workload of paediatricians | Steering committee must be convinced that reporting will not make excessive additional demands on the workload of paediatricians |
| Priority will be given to diseases that are not currently notifiable or, if notifiable, have sufficient indication of undernotification | |

## SELECTION OF STUDIES

The program is available for the study of relevant conditions of public health importance that are of such low incidence or prevalence that national ascertainment of cases is needed. To ensure maximum national representation and that sufficient numbers of cases will be generated to derive meaningful results, more than 2000 paediatricians responsible for providing health care to over six million Canadian children and youth have been enrolled as CPSP participants.

Studies for inclusion in the program are selected by the steering committee following the "Criteria for inclusion of studies" (Table 1).

Study proposals can be submitted at any time via the program coordinator and should follow the format listed in Table 2. When submissions are reviewed by the steering committee at its spring meeting, preference will be given to conditions of public health importance that have

**TABLE 2: Format for submission of proposals to the Canadian Paediatric Surveillance Program**

- Name of principal author
- Brief abstract of proposal
- Proposed starting date
- Proposed duration
- Question(s) to be addressed by study
- Statement of justification including how the information could be used
- Case definition
- Expected number of cases
- Availability of ethical approval (state source of approval)
- Funding arrangements
- Projected date for completion of analysis and submission for publication

a defined funding source. Although the program was initiated through funding from the LCDC, organizers envisage that the program will eventually assume responsibility for its own financing. This will be achieved, in part, through individual studies providing funding to cover their administrative and overhead costs. The CPSP is willing to provide limited help in obtaining funds, and assistance in coordinating arrangements for funding is available through the CPSP office.

## REPORTING METHODOLOGY

The CPSP uses a two-tier reporting methodology to ascertain and investigate cases. An initial report form (IRF) listing the conditions currently under surveillance is mailed monthly to all paediatricians actively practising in Canada. Respondents are asked to indicate, for each condition, the number of new cases seen during the previous month, including nil reports. The form is then returned to the CPSP office in a prepaid envelope provided for collation and follow-up of reported cases using a detailed report form (DRF). A section on the IRF requesting patient identifying information (for recall purposes only) and comments on the condition should be completed for each case reported. The information in this section is used to identify duplicates and is entered, as a reminder, onto a detailed report form that is sent to the original respondent to request case-specific information. The detailed report is returned to the CPSP when completed and then forwarded to the investigator for analysis. It is the responsibility of the investigator to contact the respondent if further information is required.

The DRF is developed by the investigator and must receive steering committee and ethical approval before use. For each study initiated in the program, the case definitions are sent to all potential respondents. In addition to providing a uniform basis for reporting, this approach serves to increase awareness of unusual or rare conditions. Quarterly reminders are mailed to respondents who have not replied for all months in a given period. These reminders have significantly improved response rates and the ascertainment of cases. To keep participants in the program informed of progress, maps indicating monthly compliance rates and case reports by province and territory are mailed quarterly to all participants.

**TABLE 3: Canadian Paediatric Surveillance Program – Annual average initial report form reporting rates in 1996 and 1997**

| Jurisdiction | Annual average reporting rates* 1996 | 1997 |
|---|---|---|
| British Columbia | 74% (213) | 83% (207) |
| Alberta | 79% (186) | 91% (181) |
| Saskatchewan | 61% (39) | 75% (34) |
| Manitoba | 81% (113) | 90% (108) |
| Ontario | 74% (785) | 81% (755) |
| Quebec | 75% (598) | 80% (557) |
| New Brunswick | 67% (26) | 76% (28) |
| Nova Scotia | 79% (66) | 84% (67) |
| Prince Edward Island | 79% (8) | 73% (7) |
| Newfoundland | 67% (34) | 74% (31) |
| Yukon | 100% (1) | 100% (1) |
| Northwest Territories | 96% (2) | 100% (2) |
| Overall response rates | 76% | 82% |

**Average number of physicians receiving initial report forms is shown in brackets*

A current mailing list of participants is maintained and regularly updated to reflect significant changes including the addition of new certificants and the removal of recent retirees. The main challenge, however, is to ensure that paediatricians listed on the surveillance database are currently actively practising in Canada. This is crucial because this list provides the denominator for the program's reporting rates. Paediatricians are also encouraged to report all cases fulfilling the case definitions that come to their attention. While this sometimes leads to duplicate reports, which are identified during case follow-up, it also ensures cases are not missed.

Investigators are asked to provide an annual report on the progress of their studies for the steering committee and for inclusion in the CPSP annual report. Updates on interesting findings or on program development are published in the CPS newsletter. Investigators are also encouraged to publish the results of their studies in the medical and scientific literature.

## RESPONSE BY PAEDIATRICIANS IN 1996 AND 1997

The reporting program aims to achieve a rate of return for both the IRFs and DRFs of 90% or greater, although it was recognized this could take several years. In 1996, the first (pilot) year, the overall response rate for IRFs was 76%; the highest rates were recorded in the Yukon and Northwest Territories where only one and two reporting paediatricians, respectively, were located (Table 3). The average reporting rate in the provinces with the greatest populations of reporting paediatricians – Ontario, Quebec and British Columbia – was 75%, and only one prov-

**TABLE 4: Conditions reported in 1996 and 1997**

| | 1996 | | 1997 | |
|---|---|---|---|---|
| Condition | Number of case reports on IRF | Confirmed cases | Number of case reports on IRF | Confirmed cases |
| Acute flaccid paralysis | 42 | 30 | 68 | 33 |
| Congenital rubella syndrome | 10 | 3 | 8 | 4 |
| Group B streptococcal infection of the newborn | 567 | 178 | | |
| Creutzfeldt-Jakob disease | | | 0 | 0 |
| Hemorrhagic disease of the newborn | | | 10 | 1 |
| Neural tube defects | | | 214 | 143 |
| Subacute sclerosing panencephalitis (SSPE) | | | 2 | 0* |

**Of the two reports of SSPE received, only one had consistent clinical features; however, this case initially presented in 1995 and does not therefore qualify as an incident case for 1997. Cases listed fulfilled case definition for which a detailed report was received and after duplicate or inappropriate reports were removed; IRF Initial report form*

ince, Manitoba, had a reporting rate over 80%. The rate of return of the DRFs was disappointing at 54%, although this was largely associated with the low number of returns for group B streptococcal infections in the newborn (GBS) (Table 4). In 1997, all but one province showed an increased rate of return, and the overall response rate for IRFs rose to 82%. Except for the two territories, two provinces achieved a response rate of 90% or greater while four others had an IRF return rate of 80% or greater. The return rate for DRFs increased to 89% overall. While the number of eligible paediatricians declined in 1997 as a result of enquiries to identify those physicians who saw patients, most of the increase reflected improved reporting by potential respondents.

## CONDITIONS REPORTED IN 1996 AND 1997

In the first two years of the program, seven conditions were included on the report card. Three of these – acute flaccid paralysis (AFP), congenital rubella syndrome (CRS) and GBS – were studied in the pilot year (1996). In the second year (1997), GBS was removed and four new conditions were added (Table 4). All conditions listed for 1997 were continued in 1998. The minimum period for a study is one year, although several of the conditions listed on the form will be the subject of long term investigation.

GBS was included in the first year because of a lack of Canadian data on this disease at the time. The number of reports received (567) was within the range expected. However, because several investigators are now studying perinatal infections, GBS was excluded in 1997.

The surveillance of unusual presentations or sequelae of vaccine preventable diseases has been a particular focus of the program in its first years. Polio, rubella and measles have become rare as a result of elimination programs, and surveillance has targeted unusual presentations and rare sequelae of infection (AFP, CRS, subacute sclerosing panencephalitis).

Creutzfeldt-Jakob (CJD) disease was added to the program in 1997 as part of an enhanced surveillance of this condition in Canada. CJD is extremely rare in paediatric populations, and, to date, no cases in persons under 30 years of age have been recorded in Canada (3). Worldwide, paediatric CJD is linked to transmission through human-derived growth hormone, and recent studies in Europe have identified a new variant CJD (v-CJD) characterized by young age of onset and atypical presentation (4-6). Cases of v-CJD in Europe have been linked to the consumption of beef products from cattle with bovine spongiform encephalopathy.

Hemorrhagic disease of the newborn (HDNB) was included in 1997 in response to concerns in Europe and Australia that oral vitamin K, as an alternative to intramuscular administration, may be associated with an increased incidence of late onset HDNB. This study, which is currently designed to run until December 1999, will provide much needed data on HDNB that are not available in Canada.

Surveillance systems for congenital anomalies currently exist at both provincial and federal levels in Canada (7). However, the amount of data collected is limited, and completeness of ascertainment varies. Neural tube defects reporting was included in 1997 to test a form to gather detailed descriptive information about infants who survive the early neonatal period.

More detailed descriptions of each condition under investigation, the objectives of the study and a summary of results to date are available in the CPSP Annual Reports for 1996 and 1997 (1,8).

## INTERNATIONAL DEVELOPMENTS

Since the BPSU began reporting in 1986, a number of countries have developed active paediatric surveillance programs. Modelled on the BPSU, but adapted to their own national situations, these units aim to provide a framework and methodology for case-finding for investigators who want to study rare conditions in children. The current list of surveillance units and the year that they commenced activity is presented in Table 5.

**TABLE 5: Current active paediatric surveillance units**

| Country | Year commenced | Participating paediatricians* |
|---|---|---|
| Australia | 1992 | 920 |
| Britain/Eire | 1986 | 1730 |
| Canada | 1996 | 2020 |
| Germany | 1992 | 500 |
| Latvia | 1997 | n/a |
| Malaysia | 1994 | 340 |
| Netherlands | 1992 | 420 |
| New Guinea | 1996 | 40 |
| New Zealand | 1997 | n/a |
| Switzerland | 1995 | 40 |
| Wales | 1994 | 50 |

**Approximate numbers of reporting paediatricians (based on 1996 or 1997 reports as available). Extract reproduced with kind permission of Dr Elizabeth Elliott, Australian Paediatric Surveillance Unit*

The wide diversity in conditions under surveillance by the 11 national surveillance units is illustrated by Table 6. In 1997, 45 conditions were studied; several of these – AFP, CRS, HDNB, human immunodeficiency virus/AIDS, insulin-dependent diabetes mellitus/diabetes mellitus and subacute sclerosing panencephalitis – were listed on the reporting cards of three or more units. The number of studies listed in 1997 averaged seven per unit but ranged from one to 12.

It has been proposed that the links between the existing national units be formalized by setting up an international network of paediatric surveillance units. While individual units would remain responsive to their own national requirements and priorities, the international network would promote cooperation among existing units, and provide support and assistance in the development of new units. International differences in interpretation will provide challenges in discussing topics such as case definitions, validation of results from different countries in which a variety of subspecialitists see patients, and differences in type, quality and policy for laboratory tests. Nevertheless, the development of an international network offers an exciting potential for multinational collaborative epidemiological studies using very large and diverse populations developed through the use of common research protocols. In addition, the use of common protocols will enable direct comparisons of the epidemiology and management of rare conditions in different countries and over time.

## CONCLUSIONS

In its first two years of activity, the CPSP has been established as an important program for the surveillance of rare or unusual paediatric conditions in Canada. The improvement in response rates and case ascertainment has been due to the efforts of the CPS staff, the CPSP steering

**TABLE 6: Conditions under surveillance by 11 national surveillance units**

| Disease | Unit(s) carrying out surveillance |
|---|---|
| Acute flaccid paralysis | A, C, N, NZ, PNG, S |
| Acute fulminant liver failure | M |
| Aplastic anemia | L |
| Arthogryposis multiplex congenita | A |
| Autoimmune hepatitis | G |
| Cerebral edema following DKA | BI |
| Celiac diseases | L, N |
| Congenital adrenal hyperplasia | A, PNG |
| Congenital/neonatal varicella | A |
| Congenital rubella | A, BI, C, S |
| Congenital toxoplasmosis | S |
| Esidioblastosis | L |
| Fatal and near fatal asthma | G, M |
| Group B streptococcal infections | N |
| Hemolytic uremic syndrome | BI, S |
| Hemorrhagic disease of the newborn (vitamin K deficiency bleeding) | A, C, G, S |
| Hemorrhagic shock encephalopathy syndrome | G |
| Hepatitis C infection | BI |
| Hirschsrpung's disease | A |
| Human immunodeficiency virus/AIDS | A, BI, M, N, PNG |
| Idiopathic thrombocytopenia | G |
| Insulin-dependent diabetes mellitus/ diabetes mellitus | PNG, G/L, N |
| Invasive *Haemophilus influenzae* | BI, N |
| Kawasaki disease | A |
| Leukemia | L |
| Multiple sclerosis | G |
| Neonatal herpes simplex | A |
| Neonatal meningitis | BI, M |
| Neural tube defects | C, N |
| Neurological endemic cretinism | PNG |
| Periventricular leukomalacia | S |
| Pertussis | G, N |
| Postneonatal mortality in premature and dysmature babies | N |
| Primary immunodeficiency disorders | A |
| Progressive intellectual and neurological deterioration (v-Creutzfeldt-Jakob disease)/Creutzfeldt-Jakob disease | BI/C |
| Pyriodoxine dependent seizures | BI |
| Renal tube acidosis | PNG |
| Renoleukodystrophy | L |
| Reye's syndrome | BI |
| Subacute sclerosing panencephalitis | A, BI, C, PNG |
| Systemic pneumococcal infection | G |
| Thalassaemia | PNG |
| Varicella complications | G |
| Venous thromboembolic complications | N |

*Extract reproduced with kind permission of Dr Elizabeth Elliott, Australian Paediatric Surveillance Unit. A Australia; BI British Isles; C Canada; DKA Diabetic ketoacidosis; G Germany; L Latvia; M Malaysia; N Netherlands; NZ New Zealand; PNG Papua New Guinea; S Switzerland; V Variant*

committee and, most of all, the interest of Canadian paediatricians. Through their active participation, paediatricians have indicated a growing sense of ownership of the surveillance program.

Studies of several important conditions have been established that will contribute national surveillance, eradication programs and raising diagnostic awareness. In addition, the development of an international network of paediatric surveillance units will benefit from the global sharing of information and collaborative studies across large and diverse populations. Further development of the CPSP will include increasing financial independence, the selection of a broad range of study subjects, participation in the international network, promotion of greater awareness of the program's aims and potential, and increasing case ascertainment by inclusion in the program of other speciality groups.

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