CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM

1999 RESULTS

Canadian Paediatric Society
Société canadienne de pédiatrie

Health Canada
Santé Canada

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.

For more information on the Canadian Paediatric Surveillance Program, please contact:

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Acknowledgements

This annual report of the Canadian Paediatric Surveillance Program (CPSP) provides an overview of the program to date together with surveillance summaries on the studies undertaken during 1999.

The CPSP Steering Committee would like to thank all participants, who continue to play a significant role in the collection of information on rare paediatric conditions. Their participation is the key to the CPSP's strength and success.

We would also like to thank the Laboratory Centre for Disease Control, Health Canada, whose support and insight has made these studies possible. Its commitment has allowed us to create, collect, and disseminate information to concerned Canadians.

And finally, the CPSP would like to thank the Steering Committee whose vision and inspiration has guided the program from its inception. The wealth of knowledge and leadership among its members has allowed this program to grow.

Message from the Minister of Health

As Minister of Health, I congratulate the Canadian Paediatric Society on the success of the Canadian Paediatric Surveillance Program (CPSP). The CPSP is now the largest of its kind in the world with approximately 2,300 participating paediatricians and other specialists. From its inception in 1996 when the program focused on developing and establishing surveillance in Canada, it is now firmly entrenched as a major player in the International Network of Paediatric Surveillance Units (INoPSU). The Laboratory Centre for Disease Control will be hosting the annual INoPSU business meeting in June 2000 and a scientific session on issues in paediatric surveillance.

The new century brings with it a time to reflect on past successes, and a time to boldly embrace the future. The children of today will take us forward. It is important that the paediatricians and the medical community use the knowledge generated by this program to benefit children and increase public awareness of rare conditions.

It is equally important that the partnership between Health Canada and the Canadian Paediatric Society continues in its united purpose of improving the health and well-being of Canadian children.

I am hopeful that the linkage with other paediatric surveillance units throughout the world will foster international studies on diseases of common interest. The health and well-being of children should not be constrained by 'borders'.

Canadians exemplify a caring society that values its children; it fosters and nurtures their mental and physical well-being. Accordingly, on behalf of all Canadians, I wish the Canadian Paediatric Society many years of success with the Canadian Paediatric Surveillance Program.

Allan Rock
Minister
Health Canada

Message from the Director General, Laboratory Centre for Disease Control

I am pleased to accept the fourth annual report of the Canadian Paediatric Surveillance Program. As I reflect back on these four years, I am heartened by the success of the program and its uptake by the paediatric research community.

I would like to mention one study in particular which commenced in January 2000 and exemplifies the dedication and commitment of the researchers who participate in the program and reflects the purpose of surveillance as a core public health function. The study focuses on the surveillance of cases of Smith-Lemli-Opitz syndrome, a recessive inherited defect in cholesterol synthesis causing mental retardation. The recent discovery of the biochemical defect causing the syndrome has resulted in the development of a diagnostic test and a potentially beneficial treatment. However, despite these developments, many primary care physicians remain unaware of the syndrome. Surveillance of the syndrome should lead to increased awareness which, in turn, should facilitate the identification of affected patients so that they and their families can benefit from appropriate treatment and genetic counseling.

I would like to reaffirm my commitment to the partnership between the Laboratory Centre for Disease Control and the Canadian Paediatric Society. This partnership also ensures that information obtained at the 'frontline' is conveyed to those who are in a position to take action to improve the health and well-being of the children of Canada. I am hopeful the partnership will continue to be as fruitful in the years to come as it has been since its inception.

We owe a tremendous debt of gratitude to the paediatricians of Canada for their diligence in completing the monthly surveillance 'cards' and the follow-up detailed questionnaires. The role of these frontline health care workers in diagnosing and treating these rare conditions is a vital link in the success of the program.

I would also like to extend my sincerest gratitude to the staff of the Laboratory Centre for Disease Control who have played, and who will continue to play, a critically important role in the success of the program.

Please take the time to read this report, and to understand the program and its impact on the well-being of the children of Canada.

Michael E. Shannon, MD
Director General
Laboratory Centre for Disease Control

Message from the President of the Canadian Paediatric Society

Often it is not a dramatic event that marks a shift in direction of a program, but a series of more minor, yet significant, happenings that redirect the flow of events. At the Canadian Paediatric Society (CPS), we certainly feel that the latter is true of the Canadian Paediatric Surveillance Program (CPSP), a joint program launched in partnership with Health Canada's Laboratory Centre for Disease Control in 1996. By comparing the program then and now, we can see how, several separate, yet related events have combined over the past year to reaffirm Canadian paediatric acceptance and ownership of the program, and to redefine its current focus. Clearly, such factors as the trend to more research-oriented studies by paediatric subspecialist investigators, and a gradual move to more diverse funding have also contributed to this recent change.

When the CPSP was first formed, it focused primarily on the surveillance of preventable infectious diseases, such as acute flaccid paralysis, congenital rubella syndrome, and subacute sclerosing panencephalitis. More recently, the CPSP focus has changed from validating the eradication/immunization aspects of diseases to data collection on clinical diagnosis in a cost-effective manner that will allow questions to be answered. Included in this group are such conditions as cerebral edema in diabetic ketoacidosis, anaphylaxis, and the upcoming study on hemolytic uremic syndrome.

From three initial studies in 1996 to six in 1999 and an anticipated ten in 2000, the program has steadily grown over the years. Much of the credit goes to the dedicated principal investigators, including epidemiologists, first-time paediatric surveillance investigators, and experienced, world-renowned researchers.

The CPSP has also benefited from international collaboration between investigators by exchanging surveillance definitions and protocols for the different studies, allowing global comparisons. An exciting development is on the horizon as the CPSP prepares to host the inaugural meeting of the International Network of Paediatric Surveillance Units (INoPSU). *INoPSU 2000*, a scientific symposium being held this June in Ottawa, will bring delegates from ten national units together to share their results and learn from their experiences.

Obviously, the program could not have succeeded without the ongoing committed support and faithful collaboration of all CPSP participants, including allergists, endocrinologists, medical geneticists, neurologists and paediatricians across Canada. We are grateful to all for completing the initial monthly report cards and the follow-up questionnaires. Through this maturation process, we have achieved the goal of helping children and youth by collecting data and increasing knowledge about the epidemiology of the diseases under study.

The CPS firmly believes that well conducted surveillance and research brings knowledge and educational solutions to help children and youth around the world. We wish the CPSP continued success in this important paediatric and public health endeavour.

Paul Munk, MD, FRCPC
President
Canadian Paediatric Society

CPSP Chairman's Report

With this annual report, the Canadian Paediatric Surveillance Program (CPSP) has achieved a major milestone in its maturation and development. Much of the credit must be given once again to the paediatric community at large for its continued ongoing support and participation. While voluntary completion of detailed reports providing case-specific data remains most encouraging at an overwhelming 95%, a slight decline in the initial response rate to 83% is of some minor concern.

For several years now, we have asked participants to be patient and give the program the proverbial 'chance'. This forbearance was rewarded in 1999 with an absolute bumper crop of proposals and approved new projects. Under the CPSP umbrella, the repertoire of studies further increased and, with the addition of new paediatric subspecialists, the database expanded to include more than 2,200 participants, making the CPSP the largest surveillance unit in the world. As a further testimony to the success of the program, the CPSP has in recent months received several inquiries from physicians interested in pursing similar forms of disease surveillance in other sectors.

Results from the past year have also reaffirmed that the system is working, allowing us to identify and collect critical information on these rare diseases with public health significance. For example, one Creutzfeldt-Jakob case and two subacute sclerosing panencephalitis cases were detected, when none were expected. While no new cases of hemorrhagic disease of the newborn were found in 1999, this may simply be a reaffirmation that vitamin K administration is working. Case confirmation for both acute flaccid paralysis (59) and cerebral edema in diabetic ketoacidosis (seven in six months) is on par with expected numbers.

Like our British counterparts, the CPSP has encountered several challenges with the progressive intellectual and neurological deterioration (PIND) study. Part of the difficulty may stem from the case definition encompassing so many different conditions that the criteria are unclear in the minds of participants. We may need to re-emphasize the two components of the study, namely, the counting of different confirmed diagnoses causing PIND on the one hand, and the search for PIND cases with no confirmed diagnosis on the other, in order not to miss any patients with Creutzfeldt-Jakob.

On the global front, the news is equally exciting as we eagerly prepare to host *INoPSU 2000* in Ottawa. Representatives from ten member countries of the International Network of Paediatric Surveillance Units (INoPSU) will meet to hold a methodological session, a poster presentation and a scientific symposium, challenging enhanced collaboration at a global health level.

In closing, I wish to recognize the exceptional efforts of the secretariat of the Canadian Paediatric Society, and the support of the CPSP Steering Committee and the Laboratory Centre for Disease Control, Health Canada.

Richard Stanwick, MD, FRCPC
Chairman
CPSP Steering Committee

CPSP Steering Committee 1999

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Dr. Robert Pless	Laboratory Centre for Disease Control, Health Canada
Dr. Jeff Scott	Council of Chief Medical Officers of Health
Dr. Paul Sockett	Consultant
Dr. John Watts	Canadian Paediatric Society

Published Papers Related to Studies

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Funding

The Canadian Paediatric Surveillance Program (CPSP) gratefully acknowledges the financial support of all its funders.

The highest proportion of funding is provided by the Division of Disease Surveillance, Bureau of Infectious Diseases, Laboratory Centre for Disease Control, Health Canada, to cover core administrative costs pertaining to the salary of a full-time program coordinator, and part-time salaries for administrative and financial support.

While other specific study-related expenses include the cost of Steering Committee meetings and program promotional material, undoubtedly the greatest expense is in maintaining the CPSP as an 'active' surveillance system. In the long run, however, the CPSP provides researchers with a very inexpensive means of identifying and obtaining follow-up data on cases of rare conditions and diseases.

Researchers/principal investigators interested in initiating new studies are encouraged to make early contact with the program coordinator to discuss the services provided by the program. While researchers are expected to obtain funding for their studies, the CPSP is more than willing to work with individual researchers to secure funding. Additional information on funding and the services provided by the program can be found in "How the CPSP Works" on page 37.

All sources of funding are acknowledged in the CPSP annual report. For 1999, the CPSP gratefully acknowledges funding contributions for the study on cerebral edema in diabetic ketoacidosis from:

CANADIAN DIABETES ASSOCIATION | ASSOCIATION CANADIENNE DU DIABÈTE

Children's Hospital of Eastern Ontario Research Institute
Ottawa, Ontario Canada
Institut de recherche de l'Hôpital pour enfants de l'est de l'Ontario

Overview of Program Development

Timeline

1986

Establishment of the British Paediatric Surveillance Unit

National surveillance of rare paediatric conditions had its inception in 1986 with the establishment of the British Paediatric Surveillance Unit (BPSU). The formal establishment was precipitated by the failure of paediatricians to report cases of necrotizing fasciitis, Reye's syndrome, Kawasaki disease, and hemolytic/hemorrhagic shock syndromes to the British Paediatric Association and the Public Health Laboratory Service.

1996

Establishment of a joint pilot program between the Canadian Paediatric Society and the Laboratory Centre for Disease Control

In 1995, the Canadian Paediatric Society and the Laboratory Centre for Disease Control (Health Canada) formed a small working group to set up a national paediatric surveillance program modeled on the British Paediatric Surveillance Unit. After several months of planning and consultation, a joint pilot program for the surveillance of rare paediatric diseases and conditions was established and commenced activity in January 1996. Three conditions were selected for the pilot: acute flaccid paralysis (AFP), congenital rubella syndrome (CRS), and group B streptococcal infection (GBS). AFP was selected because the CPSP provided a means of both monitoring suspected cases of paralytic poliomyelitis and providing evidence of the elimination of indigenous wild poliovirus transmission towards certification of a polio-free status in Canada and the rest of the Americas in September 1994. CRS was selected because of the need to monitor progress towards attaining the goal of elimination of indigenous rubella infection during pregnancy by the year 2000. GBS was chosen because no Canadian data existed on the incidence of the infection.

1996

Establishment of the Steering Committee

During 1996, a Steering Committee was established to ensure that the CPSP would be developed to serve the health needs of Canadian children and youth as well as the research needs of the health care community whose prime concern is the care and health of children. Membership on the Steering Committee included representation from the Canadian Paediatric Society, the Laboratory Centre for Disease Control, the Federal/Provincial Advisory Committee on Epidemiology, Chief Medical Officers of Health, and the Assembly of Canadian University Paediatric Department Heads. Also included are liaison representatives from various organizations, such as the British Paediatric Surveillance Unit, the Canadian Association of Child Neurology, and the Canadian College of Medical Geneticists.

1996

Response rate

The overall response rate of 76% was very much in line with the results of other international

surveillance units during the first year of their operations, but below the CPSP goal of 90% response.

1996

International developments

Following the success of the British Paediatric Surveillance Unit, the same methodology was adopted, and adapted in the 1990s to other countries whose paediatric services were amenable to active surveillance. By 1996/97, six other units, including Canada, had been established: Australia, Germany, the Netherlands, Switzerland and Malaysia. A meeting of the European Units was held in Leiden during January 1995 with a view to sharing and standardizing protocols, case definitions and study periods.

1996

Lessons learned

The pilot study highlighted the importance of mailing early reminders to participants who did not send in their monthly report cards, as demonstrated by response rates of 89% and 88% for January and February, respectively, compared to 61% and 64% for November and December. Three reminders were sent for the first two months while no reminders were sent for the final two months of the year. The pilot phase enabled the CPSP to evolve into a smoother, more efficient system as a result of the experience gained throughout the year.

1997

Continued growth

The CPSP continued to grow and build in 1997. Three additional diseases were added to the program: Creutzfeldt-Jakob disease, hemorrhagic disease of the newborn and neural tube defects. At the same time, surveillance of group B strep was discontinued, partly in response to an increase in the number of investigators who had commenced studies on GBS following the publication of guidelines for the management of GBS during pregnancy and delivery. Initial overall response rates by paediatricians climbed significantly from 76% in 1996 to 82% in 1997. Follow-up rates for detailed reporting forms improved from 54% in 1996 to 89% in 1997.

A poster presentation at the Canadian Paediatric Society's (CPS) annual meeting profiled the evolution of the CPSP and its findings to date. The presentation provided CPS members with the opportunity for direct feedback on current and future directions of the program.

On the international scene, Latvia and New Zealand established national paediatric surveillance units.

1998

Increased self-direction

While no new studies were added to the CPSP, surveillance of neural tube defects concluded in 1998. The program continued to evolve becoming more self-directed, as in the summer of 1998 a call was issued for research proposals. The call was successful with six additional new studies approved for inclusion in the program pending confirmation of financial support and ethical approval: anaphylaxis, cerebral edema in diabetic ketoacidosis, idiopathic interstitial lung disease, perinatal hemochromatosis, pyridoxine-dependent status epilecticus, and vitamin D-deficiency rickets. With more than 2,100 paediatricians participating in the program, the CPSP became the largest paediatric surveillance unit in the world.

The response rate for initial reports was 86%, a slight increase over the 1997 rate of 82%. Detailed reporting forms were received for 93% of the 258 cases reported in 1998.

The British Paediatric Surveillance Unit requested that Canada serve as a control for one of its studies; consequently, the study on the surveillance of Creutzfeldt-Jakob disease was expanded to include cases of progressive, intellectual and neurological deterioration. At the same time, the CPSP welcomed the participation of child neurologists for this study through a partnership with the Canadian Association of Child Neurology.

In August 1998, during the 22nd International Congress of Paediatrics in Amsterdam, the International Network of Paediatric Surveillance Units (INoPSU) was formed. The founding units were: Australia, United Kingdom, Canada, Germany, Latvia, Malaysia, the Netherlands, New Zealand, Papua New Guinea, and Switzerland. The CPSP invited INoPSU to host its first scientific meeting during the Canadian Paediatric Society's annual meeting in June 2000, affording Canadian paediatricians an excellent opportunity to benefit first-hand from this research dissemination.

1998

Lessons learned

Final study results on neural tube defects indicated that case ascertainment was incomplete. In retrospect, it became clear that establishing a network of collaborators is of prime importance when studying the occurrence of conditions that involve a number of health care professionals. To ensure that case ascertainment is complete, all collaborators must be involved. In this case, extending the list of participants to include other subspecialities, such as obstetricians and neonatologists, would have ensured that case ascertainment results were more complete.

1999

CPSP gains recognition

The CPSP has started to gain recognition among paediatric researchers as the number of queries about the program increased throughout the year. A number of new studies have been approved and will commence in 2000: anaphylaxis and Smith-Lemli-Opitz on January 1, hemolytic uremic syndrome with diarrhea and without on April 1, and neonatal herpes on September 1 (tentative). Paediatric subspecialists in allergy, medical genetics, and intensive care will be added as participants in the program for these new studies. Two letters of intent have been received for surveillance studies on primary pulmonary hypertensive angiopathy and lead toxicity.

The International Network of Paediatric Surveillance Units met during the British Paediatrics and Child Health meeting in Edinburgh, Scotland, in November 1999. Luxembourg and Belgium expressed interest in establishing national paediatric surveillance units.

1999

Lessons learned

Overall, study results from 1999 were most encouraging. Not only were cases of such rare conditions as Creutzfeldt-Jakob disease and subacute sclerosing panencephalitis found, but CPSP participants, recognizing the importance of the program, completed and returned a record number of questionnaires, providing investigators with valuable detailed case-specific data. The CPSP has even received queries recently about whether similar counterpart surveillance systems exist in other areas of health care.

Surveillance Studies in 1999

Acute flaccid paralysis

Highlights

- Acute flaccid paralysis (AFP) surveillance is contributing to the documentation of global polio eradication necessary to be able to discontinue systematic polio vaccination in the foreseeable future.
- In 1999, our AFP study met the internationally targeted rate of one case per 100,000 in children under 15 years of age expected to occur in the absence of wild polio.
- While the number of cases in whom polio-specific laboratory investigations were reported has improved over previous years, it remains significantly lower than the World Health Organization's (WHO) targeted rate.
- **It is strongly recommended** that in ***all*** AFP cases a stool specimen be collected within two weeks of onset of paralysis for isolation of wild or vaccine strain poliovirus.

> *"The Pan American Health Organization (PAHO) was impressed by our successful system of identifying, reviewing and investigating all AFP cases.*
>
> Dr. Paul Varughese

Summary

Fifty-nine confirmed AFP cases, with a mean age of seven years, were reported to the CPSP in 1999; this is equivalent to the minimum estimated background rate of one case per 100,000 population less than 15 years of age.

The number of cases in 1999 represents a 40% increase over the number of cases reported in an equivalent reporting period for 1998, indicating continued improvement in reporting. As in previous years, the majority (83.1%) of cases were diagnosed Guillain-Barré syndrome, followed by transverse myelitis (10.2%). Of note, the proportion of AFP cases in whom an adequate stool investigation for isolation of poliovirus or other enterovirus was reported has increased over previous years; however, it remains lower than the WHO recommended and targeted rate of 80%. It is worth reminding paediatricians and paediatric neurologists that the single most important laboratory investigation is a stool specimen collected within two weeks of onset of paralysis for screening for wild or vaccine strain poliovirus, and that negative results of polio-specific investigations are as important as positive results for the evaluation of AFP cases.

Background

The elimination of indigenous wild poliovirus transmission in Canada, and the rest of the American region, was certified in September 1994. However, until global polio eradication is attained there remains an ongoing risk of wild poliovirus importation from polio-endemic regions to Canada. Consequently, active surveillance of AFP in children less than 15 years of age is used to monitor potential cases of paralytic poliomyelitis. Based on an estimated background annual incidence of one case per 100,000 population less than 15 years of age in the absence of wild poliovirus transmission,[1] the estimated minimum number of AFP cases in Canada is 60 cases per year. AFP surveillance in Canada was initiated in 1991 through the

TABLE 1

Age distribution of AFP cases reported to the CPSP, 1996-1999

Age group (years)	Number of cases (%)			
	1996	1997*	1998**	1999
0 – 1	2 (6.7)	0	2 (4.7)	2 (3.4)
2 – 5	11 (36.7)	13 (37.1)	15 (34.9)	18 (30.5)
6 – 10	9 (30.0)	12 (34.3)	18 (41.9)	23 (39.0)
11 – <15	8 (26.7)	10 (28.6)	8 (18.6)	16 (27.1)
Total	**30**	**35**	**43**	**59**

* Includes two delayed reports not included in the *1997 CPSP Results*

** Includes two delayed reports not included in the *1998 CPSP Results*; based on cases with age specified

IMPACT (Immunization Monitoring Program ACTive) network of paediatric tertiary care centres, and since 1996 has been implemented through the CPSP. This report presents the results of AFP surveillance in 1999 and compares them to those from previous years.

Objective

The objective of AFP surveillance is to identify AFP cases (including Guillain-Barré syndrome) in children less than 15 years of age to rule out paralytic poliomyelitis, and thereby monitor the polio-free status of Canada.

Case definition

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

Duration

January 1996 to December 2004

Methods

Surveillance is based on reporting by paediatricians and active monitoring of hospital admissions to the 12 IMPACT centres. Paediatricians submit initial monthly reports of the number of cases seen, followed by detailed reports of case-specific information using a standardized reporting form. AFP cases detected through IMPACT are also reported to the CPSP using the same reporting form. The Health Canada study investigator reviews case-specific information and refers cases compatible with suspected paralytic poliomyelitis case definitions to the national Working Group on Polio Eradication for further review.

Results

In 1999, the CPSP received 113 initial AFP reports, of which 54 (47.8%) were discarded. They included 43 duplicate reports and 11 cases that did not meet the AFP surveillance case definition (eight cases ≥15 years of age, and three that were diagnosed as an acute viral encephalitis with bilateral sixth cranial nerve paralysis, an ischemic stroke, and a tick paralysis).

Of the remaining 59 confirmed AFP cases, 38 (64.4%) were male and 21 (35.6%) were female. The cases ranged in age from five months to

14.7 years (mean of 7.0 years). Table 1 shows the age distribution of AFP cases reported in 1999 compared with cases reported from 1996 to 1998.

Overall, the age distribution is similar throughout the reporting period. Thirty-one (52.5%) of the 59 cases in 1999 had received age-appropriate polio immunization, the immunization information reported for five cases (8.5%) was incomplete for their ages, and 23 cases (39.0%) had no available polio immunization history.

Adequate stool investigation for the isolation of poliovirus or non-polio enteroviruses (i.e., stool specimen collected within two weeks of the onset of paralysis) was reported for 25 (42.4%) of 59 cases; 16 of those were negative for poliovirus and other enteroviruses; however, the result is unknown for nine cases. Among cases for whom a stool investigation was not carried out, nine cases (15.3%) had throat and/or cerebrospinal fluid specimens collected for viral isolation; none were reported as positive for poliovirus or other enteroviruses. None of the cases had paired serological tests for polio-specific antibody titres performed; two cases had single tests reported, but with inconclusive results. Overall, 25 cases (42.4%) did not have adequate polio-specific laboratory investigation reported. As in previous years, neurological investigations were reported for the majority (52 or 88.1%) of the 59 AFP cases. These tests consisted of at least one of nerve conduction studies, electromyography, MRI, or CT scan; abnormal findings compatible with the neurological diagnosis were reported for one or more of the tests done for 40 (76.9%) cases.

The final neurological diagnosis was reported as Guillain-Barré syndrome in 49 cases (83.1%) and transverse myelitis in six (10.2%) (Table 2). The remaining four diagnoses included plexitis (2), brachial neuritis and rhombomyelitis. Fifty-six cases (94.9%) were hospitalized for periods ranging from two to 87 days (mean of 12 days); three cases were hospitalized for 30 days or

TABLE 2

Neurological diagnosis of AFP cases reported to the CPSP, 1996-1999

Final Diagnosis	Number of cases (%)			
	1996	1997*	1998**	1999
Guillain-Barré syndrome	21 (70.0)	29 (82.9)	34 (77.3)	49 (83.1)
Transverse myelitis	6 (20.0)	2 (5.7)	6 (13.6)	6 (10.2)
Encephalitis/encephalomyelitis/encephalopathy	1 (3.3)	1 (2.9)	1 (2.3)	0
Myelopathy	0	1 (2.9)	0	0
Radiculopathy/radiculoneuritis	1 (3.3)	1 (2.9)	0	0
Plexitis/lumbosacral plexitis	0	0	0	2 (3.4)
Brachial neuritis	0	0	0	1 (1.7)
Rhombomyelitis	0	0	0	1 (1.7)
Not specified/undetermined diagnosis or etiology	1 (3.3)	1 (2.9)	3 (6.8)	0
Total	**30**	**35**	**44**	**59**

* Includes two delayed reports not included in the *1997 CPSP Results*

** Includes two delayed reports not included in the *1998 CPSP Results*

longer. Of the total of 59 cases, 12 (20.4%) were fully recovered at 60 days after the onset of paralysis, five (8.5%) had recovered partially with residual weakness, and two (3.4%) had a stable or progressive condition. Among the remaining 38 cases whose recovery status was unknown at 60 days after the onset of paralysis, 27 had recovered partially on initial discharge or reporting.

Discussion

The 59 AFP cases identified in 1999 represents a 40% increase compared to 42 cases reported in 1998 (excluding delayed reports). It is encouraging to note that the AFP reporting rate has improved since the introduction of paediatrician-based reporting through the CPSP from 0.5 per 100,000 children under 15 years of age in 1996 (30 cases) to one case per 100,000 in 1999 (59 cases). The 1999 AFP rate, in fact, is equivalent to the minimum background rate of AFP expected in the absence of wild poliovirus circulation and, therefore, reflects a high level of sensitivity of the current surveillance system. It also supports previous observations that the expansion of AFP surveillance to the CPSP has improved the completeness of surveillance, by ensuring that AFP cases seen at non-tertiary hospitals are reported, in addition to those cases admitted to paediatric tertiary care hospitals, which were previously reported through IMPACT.

It is also significant that in 1999, 100% of the detailed case-specific information forms were completed and returned for all AFP case reports. This marks the first time a complete return rate has been recorded since the inception of the CPSP; the return rate for case-specific information in previous years was 79% in 1996, 96% in 1997 and 97% in 1998. Although duplicate reporting remains relatively high, in many instances the duplication provided additional information not included in the 'primary' report, thereby proving to be very useful. Therefore, all participating paediatricians, paediatric neurologists and IMPACT monitors are still encouraged to submit detailed reporting forms, even when they suspect a case to be a potential duplicate, unless there is a clear indication that the information reported would be the same (e.g., where there is a designated reporter among a group of paediatricians in the same practice).

Areas for improvement

A major area in which AFP surveillance could be improved is the performance of polio-specific investigations and reporting of results. The proportion of cases in whom polio-specific laboratory investigations were reported remained low in 1999. Specifically, only 42% of cases had an adequate stool investigation. However, this is an improvement over previous years (33% in 1996, 37% in 1997 and only 25% in 1998) but remains significantly lower than the World Health Organization targeted rate of adequate stool investigation in 80% of AFP cases. In addition, the results of stool investigation are unknown for almost a third of those tested. While neurological investigations provide supporting evidence for the final diagnosis in the majority of reported AFP cases, polio-specific laboratory investigations remain vital for the evaluation of ***all*** cases, including those in whom poliomyelitis is not being considered as a possible diagnosis. Negative results of appropriate polio-specific investigations are as important as a positive result would be in AFP case evaluations. The single most important laboratory investigation, recommended by the national Working Group on Polio Eradication, to confirm or to rule out a diagnosis of paralytic poliomyelitis, is a stool specimen collected within two weeks of onset of paralysis for isolation of wild or vaccine strain poliovirus; specimens may be collected up to six weeks after the onset of paralysis, although after two weeks the sensitivity of virus isolation decreases.[2] The examination of paired

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

Acknowledgements

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Funding

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Cerebral edema in diabetic ketoacidosis

Highlights

- Seven cases of cerebral edema in diabetic ketoacidosis (CE-DKA) were confirmed during the six-month period from the start of the study on July 1, 1999 until the end of the year.
- One patient died during an episode of DKA. No other mortalities in children/teens with diabetes were reported from causes other than DKA.
- The inclusion criteria have been revised to be more inclusive, since at least two cases of CE at presentation and another two of profound lethargy had no clear deterioration. Please refer to the case definitions below.
- Imaging remains a very useful diagnostic tool to confirm CE in DKA patients with profound lethargy, change in level of consciousness and coma.

"Cerebral edema is a devastating complication of diabetic ketoacidosis. To ensure that patients with CE are not missed, we have revised the inclusion criteria to cast a wider net.

Dr. Sarah Muirhead

Background

Cerebral edema, or brain swelling, is a devastating complication of diabetic ketoacidosis (DKA) in the paediatric age group, resulting in a

high rate of mortality or survival with permanent neurological damage. Studies to date have failed to clearly establish risk factors for cerebral edema. The aim of this study is to identify the frequency of this condition in Canada. Through a case-control study, the aim is to identify risk factors that can then be used to develop a modified treatment regimen for DKA.

Objectives

1. To determine the incidence of cerebral edema in association with DKA.
2. To identify risk factors for cerebral edema in association with DKA.
3. To determine the outcome of cerebral edema in association with DKA.
4. To determine other causes of death in children and youth with diabetes not related to DKA.

Case definitions

A. Inclusion criteria

1. Age of less than 16 years old.
2. Type 1 or 2 diabetes mellitus.
3. Diabetic ketoacidosis (DKA) defined as a pH <7.35 and/or bicarbonate below the normal range for the local laboratory in association with diabetes and ketonuria.
4. Cerebral edema defined as a sudden or unexpected deterioration in level of consciousness. **Also to be considered are patients with no deterioration, but coma at presentation or profound depression of level of consciousness during treatment.**
5. Any death in a child with Type 1 or 2 diabetes, either during or unrelated to an episode of DKA.

B. Exclusion criteria

Deterioration in level of consciousness associated with hypoglycemia and responsive to glucose administration.

Duration

July 1999 to June 2001

Methods

To determine the incidence of cerebral edema in DKA, cases of cerebral edema are identified through the Canadian Paediatric Surveillance Program (CPSP) and compared to the number of DKA cases in the Canadian Institute for Health Information (CIHI) database. A case-control study nested within the surveillance study will follow with detailed chart reviews of two groups – all cases of cerebral edema, as well as controls (DKA with no cerebral edema) – to look for differences in presentation and management between the two groups.

Results

A total of 11 reports were received during the first six months of surveillance, four of which were duplicates. Five of the remaining seven reports were confirmed cases, and two were probable cerebral edema. The mean (SD) age was 8.9 (5.7) years with a range of 1.1 to 15 years. Cerebral edema was the initial presentation of diabetes in five cases, and one was unspecified.

Of the seven cases, two had a Glascow Coma Scale of three and were presumed CE on presentation (i.e., pre-treatment) and later confirmed with a CT scan. Two others did not have a specific deterioration in level of consciousness, but one was more profoundly lethargic than would be expected for the degree of acidosis, and the other had a prolonged period of neurological recovery. The remaining three children deteriorated from one to six hours after the initiation of treatment.

In five of the cases, the outcome was normal upon discharge. One patient, however, was reported as having generalized weakness and an unsteady gait ten days after the episode of CE,

while another died, having deteriorated within six hours of presentation and treatment. To date, no reports have been received of children and youth with diabetes dying from alternative causes other than DKA.

Summary

The number of seven confirmed cases in six months falls within the anticipated rate of 16 cases per year. These cases include children with evidence of cerebral edema at presentation and those with much more profound or prolonged CNS depression than would be expected for the degree of acidosis. Imaging can be very helpful in these situations. Although some of the cases do not strictly meet our current inclusion criteria, they have proven to be very important in gaining insight into this condition. As a result, the inclusion criteria have been revised in the case definitions cited above to cast a wider net, so as not to miss any patients (see bolded text). Some reports may, however, be excluded as the process continues.
We would like to thank all CPSP participants for their contribution to the CE-DKA surveillance program.

Funding

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Congenital rubella syndrome

Highlights

- Only one infant born with congenital rubella syndrome (CRS) was reported to the CPSP in 1999. The mother of the infant had a documented history of rubella immunization in Canada and was not aware of having clinical rubella during her pregnancy.
- From 1996 to 1999, one or two newborns with CRS per year were reported to surveillance systems in Canada (0.3 to 0.5 per 100,000 births).

> *Successful rubella immunization programs continue to result in very few cases of CRS in Canada.*
> Dr. Paul Varughese

Background

In Canada, rubella immunization programs were introduced in the 1970s. However, the program strategies varied; some provinces initially opted for selective immunization of pre-adolescent females, and others opted for immunization of all infants. By 1983, all provinces and territories across Canada had implemented routine measles-mumps-rubella combined vaccine (MMR) at 12 months. During 1996 and 1997, all provinces and territories introduced a routine second dose MMR or measles-rubella combined vaccine (MR) given at 18 months or four to six years of age.

Since 1970, the incidence of rubella in Canada has declined markedly; fewer than 100 cases were reported annually in the past two years. During a national consensus conference in 1994, a goal of eliminating indigenous rubella infection during pregnancy by the year 2000 was established.

In Canada, passive reporting of CRS to the Notifiable Diseases Reporting System (NDRS) began in 1979. Active surveillance of CRS began in 1992 through a network of 12 tertiary care paediatric hospitals (representing more than 85% of paediatric tertiary care beds in Canada) participating in IMPACT (Immunization Monitoring Program ACTive). Since 1996, IMPACT cases have been forwarded to the CPSP. Paediatricians surveyed in the CPSP were also asked to report newborns with laboratory-confirmed congenital rubella infection (CRI) without obvious manifestations at birth.

Objectives

1. To estimate the incidence of congenital rubella syndrome and congenital rubella infection in Canada.
2. To obtain detailed epidemiological data, including maternal histories, on reported cases of congenital rubella syndrome and infection.

Methods

From January 1996 to December 1999, physicians or IMPACT investigators reporting CRS and CRI cases through the CPSP were asked to complete detailed report forms. If more than one physician reported on a particular case, the information from all case report forms was reviewed and collated. Provincial and territorial public health authorities were consulted to determine if cases had been previously reported.

Case definitions

Confirmed case of CRS

Live birth:
Two clinically compatible manifestations (any combination from Table 1, Columns A and B) with laboratory confirmation of infection:

- isolation of rubella virus from an appropriate clinical specimen;

or

- detection of rubella-specific IgM (in the absence of recent immunization with rubella-containing vaccine);

or

- rubella-specific IgG persisting at elevated levels for longer than would be expected from passive transfer of maternal antibody, or in the absence of recent immunization.

Stillbirth:
Two clinically compatible manifestations with isolation of rubella virus from an appropriate clinical specimen.

Note: The following cannot be classified as a CRS case:

- rubella antibody titre absent in the infant;

or

- rubella antibody titre absent in the mother;

or

- rubella antibody titre declining in the infant consistent with the normal decline after birth of passively transferred maternal antibody.

TABLE 3

Congenital rubella syndrome: clinically compatible manifestations of congenital rubella syndrome

Column A	Column B
1. Cataracts or congenital glaucoma (either one or both count as one)	1. Purpura
2. Congenital heart defect	2. Hepatosplenomegaly
3. Sensorineural hearing loss	3. Microcephaly
4. Pigmentary retinopathy	4. Micro-ophthalmia
	5. Mental retardation
	6. Meningoencephalitis
	7. Radiolucent bone disease
	8. Developmental or late onset conditions such as diabetes and progressive panencephalitis and any other conditions possibly caused by rubella virus.

Congenital rubella infection (CRI)

Confirmed case

A case with laboratory confirmation of infection but with no clinically compatible manifestations:

- isolation of rubella virus from an appropriate clinical specimen;

or

- detection of rubella-specific IgM in the absence of recent immunization with rubella-containing vaccine;

or

- persistence of rubella-specific IgG at elevated levels for longer than would be expected from passive transfer of maternal antibody, or in the absence of recent immunization.

Rubella in clinical illness

Confirmed case

Laboratory confirmation of infection in the absence of recent immunization with rubella-containing vaccine:

- isolation of rubella virus from an appropriate clinical specimen;

or

- significant rise in serum rubella IgG antibody level by any standard serologic assay;

or

- positive serologic test for rubella-specific IgM;

or

- clinical* illness in a person who is epidemiologically linked to a laboratory-confirmed case.

Results

In 1999, only one case of CRS was identified both by NDRS and the CPSP. The infant was born with intra-uterine growth retardation, congenital cataract, patent ductus arteriosus, pulmonary stenosis, ventricular/atrial septal defect and microcephaly. Rubella virus was cultured from the baby's urine and throat specimens at three months of age, and serology done at the same time was positive for rubella-specific IgM and IgG.

The child's 26-year old Canadian-born mother, a primigravida, received MMR vaccination in May 1973. This was supported with written documentation. She did not recall having any contact with a rubella case or having any symptoms compatible with rubella during pregnancy. She reported having visited Mexico when she was four weeks pregnant. Routine rubella IgG screening done on the mother at 15 weeks gestation, as part of her prenatal care, was positive for IgG by ELISA (optical density greater than 2.5). However, following the diagnosis of congenital rubella syndrome in her child, an IgM test done on the serum collected at 15 weeks was weakly positive.

Discussion

The 1999 case history indicates that the mother received the vaccine about 25 years prior to the infection with rubella, but it failed to provide protection against the disease. This suggests either a primary or secondary vaccine failure. Generally, one dose of rubella vaccine is considered to be protective in 98% to 99% of susceptibles.[1] There are still unanswered questions about the duration of protection afforded by rubella vaccines (one dose), and concern has been raised about the possibility of declining levels of immunity in previously vaccinated populations.[2] In the absence of circulating rubella in Canada, it is possible that the mother could have been infected in Mexico where rubella activity continues to be

* *Clinical illness is characterized by fever and rash, and at least one of the following: arthralgia/arthritis, lymphadenopathy, conjunctivitis. Up to 50% of rubella infections are reported to be subclinical.*

TABLE 4

Cases of CRS by year of birth reported to CPSP/IMPACT and NDRS, January 1996 to December 1999

Year of birth	Reported to NDRS only	Reported to CPSP only	Reported to both NDRS and CPSP	Total
1996	1	0	1	2
1997	0	0	1	1
1998	0	0	1	1
1999	0	0	1	1
Total	**1**	**0**	**4**	**5**

NDRS data is provisional

very high; routine vaccination with MMR was introduced in that country only as recently as 1998.

From January 1996 to December 1999, with active surveillance in place, four new reports of newborns with CRS were reported in Canada (Table 4). Two were born to immigrant women, one to an aboriginal Canadian mother and one to a non-aboriginal Canadian. These four cases illustrate the need for documentation of previously received rubella vaccination, of maternal immunity status, and postpartum rubella vaccine when indicated.

Health care providers are requested to ensure that all women without documented proof of rubella immunization receive the vaccine. Special attention should be given to the review of vaccination records of women from regions with poor vaccination coverage, including women in immigrant populations. Routine rubella antibody screening antenatally is central to the congenital rubella prevention strategy and all women found to be susceptible should be vaccinated in the immediate postpartum period. **Standing orders for vaccination of susceptible women before discharge from hospital is the most effective way to ensure that the opportunity is not missed.**

The degree of under-diagnosis and under-reporting for CRI, CRS with less severe manifestations, and CRS with delayed-onset manifestations is unknown. So far, no cases of CRI have been reported to the CPSP. Physicians are reminded that it is important to investigate all infants born to mothers who have confirmed or suspected rubella infection during pregnancy, even if the infants have no obvious abnormalities on examination.

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Hemorrhagic disease of the newborn

Highlights

- No confirmed cases of hemorrhagic disease of the newborn were reported to the Canadian Paediatric Society Surveillance Program (CPSP) in 1999.
- An audit with the Canadian Association of Pediatric Hospitals (partially complete) reveals no cases of hemorrhagic disease of the newborn reported in 1999.

"Newborns with abnormal bleeding need an appropriate 'workup', including coagulation studies.

Dr. Douglas McMillan

Background

Hemorrhagic disease of the newborn (HDNB) is characterized by unexpected bleeding, often with gastrointestinal hemorrhage, ecchymosis and, in severe cases, intracranial hemorrhage. Early HDNB, occurring within the first 24 hours of life, is uncommon and usually occurs in babies born to mothers taking drugs that impair vitamin K metabolism (e.g., anticonvulsants, antituberculous medications). Classical HDNB (occurring the first week of life) is rarely seen when vitamin K is appropriately given to newborn infants. Late HDNB (three to eight weeks of age) occurs primarily in breastfed babies with limited oral intake of vitamin K. It may be associated with death or neurologic sequelae in 50% of the babies in which this occurs.

In 1997, the Canadian Paediatric Society (CPS) and the College of Family Physicians of Canada published revised guidelines on the administration of vitamin K to newborn babies.[1] Based on concerns from Germany, Britain, Sweden, and Australia that the use of oral vitamin K may be associated with increased incidence of late HDNB, the CPS recommends intramuscular vitamin K be the usual standard for newborn babies following birth.

Objective

Inclusion of HDNB in the Canadian Paediatric Surveillance Program helps to identify the incidence of HDNB in the Canadian population and the relationship of vitamin K administration following birth. This will assist in assessing the impact of CPS recommendations in this area.

Case definition

Abnormal bleeding in the first three months of life associated with an abnormal prothrombin time of >18 seconds or an INR (international normalized ratio) of >1.4 without other abnormalities of coagulation or explained by another diagnosis of liver, bowel or systemic disease.

An article was published in *Paediatrics & Child Health* in 1998 to assist practitioners in differentiating vitamin K deficiency producing HDNB from other causes of bleeding in the newborn.[2]

Duration

January 1997 to December 2002

Methods

The program coordinator or the principal investigator follows up reports to the CPSP with requests for further information to confirm or refute the diagnosis of HDNB.

Results

Of the five reports received in 1999, three were discarded as reporting errors (actually hemolytic disease of the newborn), and two were discarded for not meeting the diagnostic criteria (coagulation studies were normal).

An abstract entitled "Reports of hemorrhagic disease of the newborn (HDNB) to the Canadian Paediatric Surveillance Program (CPSP) – Frequency, errors and relationship to vitamin K" will summarize 1997-1999 reports in a poster session at the 2000 Annual Meeting of the Canadian Paediatric Society in Ottawa in June.

The CPSP has been working in association with the Canadian Association of Pediatric Hospitals to confirm reports in all studies. For HDNB, medical records departments at five Canadian children's hospitals confirmed that they had no reported cases. This is partial confirmation that no cases of HDNB were reported to the CPSP because they did not occur.

Conclusions

- There were no confirmed reports of HDNB in 1999.
- These results reinforce that administration of vitamin K to newborn babies is working.
- Reports of hemolytic disease of the newborn continue to be confused with hemorrhagic disease of the newborn, possibly because of the common abbreviation of HDNB.
- Collaboration with the Canadian Association of Pediatric Hospitals will provide a mechanism to ascertain the validity of reports to the CPSP.
- Paediatricians and others caring for newborns with abnormal bleeding are reminded of the need for an appropriate 'work up', including coagulation studies.[2]

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Progressive intellectual and neurological deterioration in paediatric populations

Highlights

- One iatrogenic Creutzfeldt-Jakob disease (CJD) case was documented in the paediatric age group.
- CPSP participants need a better understanding of the two different components of the PIND study: counting the incidence of confirmed PIND cases with a known diagnosis, and evaluating (expert panel) PIND cases with an unknown diagnosis (see Tables 6 and 7).

"Progressive intellectual and neurological disorders (PIND) are rare disorders in which there is clinical evidence of regression or loss of motor skills, as well as cognitive abilities already obtained, and should not be confused with static encephalopathies.

Dr. Daniel Keene

Background

An enhanced active surveillance system for progressive intellectual and neurological deterioration (PIND) was implemented to detect, prospectively, among the Canadian paediatric population, all persons with neurological conditions defined by a common presentation of progressive intellectual and neurological deterioration. Participating paediatricians and neurologists used a standard screening definition for PIND. The principal investigator reviewed all reported cases and classified them into one of four predetermined categories. Cases with evidence of neurological and intellectual regression without a known cause were reviewed by a panel of paediatric experts. Reported cases were also reviewed for the possibility of classic or variant Creutzfeldt-Jakob disease (vCJD). If the review panel felt that a reported case might have this disorder, it was referred to the CJD-Surveillance System Canada (CJD-SSC) team for further investigation. Cases referred to CJD-SSC were to be monitored throughout their lives and investigated at death, unless elements of the case warrant earlier investigation.

Objectives

1. To conduct active surveillance of the Canadian paediatric population for neurological conditions that are defined by a common presentation: progressive intellectual and neurological deterioration.
2. To investigate all reported cases of PIND to detect any cases of CJD or vCJD occurring in paediatric populations in Canada.
3. Upon identification of any case of CJD or vCJD, to conduct further investigation by enrolling the case in CJD-Surveillance System Canada.

Case definition

Any child less than or equal to 18 years of age who fulfills all of the following conditions: progressive deterioration for more than three months with loss of already attained intellectual/developmental abilities **and** development of abnormal neurological signs.

Inclusion criteria

Progressive deterioration for more than three months in a child less than or equal to 18 years of age,

with

loss of already attained intellectual and developmental abilities,

and

development of abnormal neurological signs.

Include (even if specific neurologic diagnoses have been made):

- Metabolic disorders leading to neurological deterioration.
- Seizure disorders if associated with progressive deterioration.
- Children who have been diagnosed as having neurodegenerative conditions, but who have not yet developed symptoms.

Exclusion criteria

Static intellectual loss, e.g., after encephalitis, head injury or near-drowning.

Duration

July 1999 to June 2001

Methods

On a monthly basis clinicians were asked to report cases of progressive intellectual and neurological deterioration in children to the CPSP. Once a case was reported to the CPSP, a standardized questionnaire was sent to the treating physician requesting clinical data. If the patient had already been seen and diagnosed by a paediatric neurologist, only the diagnosis (along with the patient's date of birth and sex to eliminate duplicate reports) was requested. If a clinical diagnosis had not been made, information regarding the clinical history, progress of the disorder, and results of laboratory investigations was requested. The principal investigator reviewed the data and classified the patients into one of the following four groups:

- Group A consisted of patients with clinical evidence of progressive intellectual and neurological deterioration and sufficient information to make a diagnosis.
- Patients in Group B had a history compatible with the diagnosis of either the classic or variant forms of Creutzfeldt-Jakob disease and were referred to CJD-Surveillance System Canada for further investigation and follow-up.
- Group C consisted of patients with clinical evidence of progressive intellectual and neurological deterioration for which an adequate reason was not available. These patients were referred to a panel of paediatric neurologists and neuropathologists for possible classification.
- Group D consisted of patients who were referred to the study, but did not meet the criteria for entry.

An additional group, designated as Group U, was created for cases still under investigation and awaiting further information from referring clinicians prior to classification.

Results

In the six-month period from the start of the study on July 1, 1999, the CPSP received 41 reports of possible cases of progressive neurological and intellectual deterioration. Five of these reports ultimately proved to be duplicates. The reporting rate remained fairly consistent over this six-month period, except for the month of October when there was a

noticeable increase in case reports, perhaps due to the mailing of a fact sheet on the study to all physicians.

The breakdown of case reports from across the country was fairly representative of Canada's population density, with the highest number coming from Ontario (21) and the smallest number from the Prairie provinces (one each). The Atlantic region reported nine cases, Quebec four and British Columbia four. Physicians reporting cases tended to be mainly community-based paediatricians (25 cases). Paediatric neurologists reported eight cases. To date, all reported cases have been seen in one of the major teaching centres by a paediatric neurologist.

Nineteen cases were felt to have a progressive intellectual and neurological deterioration that was not due to Creutzfeldt-Jakob disorder. (See Table 6 for specific diagnosis.) One case of iatrogenic Creutzfeldt-Jakob disorder was reported in a 13-year-old child who had a duroplasty done several years prior to presenting with symptoms of behaviour changes with neurological regression. This case was also reported independently to CJD-Surveillance System Canada. No cases of the variant form of CJD were found during this survey period. Seven cases were excluded from this study, as clear evidence of neurological and intellectual regression was felt not to be present. These cases represented static encephalopathies. (See Table 7.) Nine cases could not be classified due to lack of information.

Summary

Cases meeting the criteria for entry into this study have accrued at the expected rate. One case of iatrogenic CJD was reported to this study, but it had also been reported to CJD-

TABLE 6

Diagnosis of patients meeting entry criteria to PIND study

Mitochondrial disorders	6
Krabbe's disorder	4
Cree encephalopathy	2
Rett syndrome	1
Adrenoleukodystrophy	1
Hurler's syndrome	1
Gaucher's disease type IV	1
Fumerase deficiency	1
Mucopolysaccharidosis type pending	1
Iatrogenic methotrexate encephalopathy	1

TABLE 7

Diagnosis of patients not meeting entry criteria to PIND study

Mental retardation of unknown etiology without evidence of intellectual and neurological regression	3
Patient with a documented chromosomal abnormality without intellectual and neurological regression	1
Patient with a refractory epilepsy and mental retardation without intellectual and neurological regression	1
Patient with documented moya-moyo disorder without intellectual and neurological regression	1
Patient with axonal motor neuropathy without intellectual regression	1

TABLE 8

Summary of reported PIND cases

PIND	19
CJD	1
Duplicates	5
Discards	7
Insufficient data	9
Total	**41**

Surveillance System Canada. No new cases of CJD were identified from within the PIND-referred group of patients. This study adds supportive evidence for the complete ascertainment for the CJD-Surveillance System in childhood and adolescence.

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Subacute sclerosing panencephalitis

Highlights

- Between 1995 and 1998, no cases of subacute sclerosing panencephalitis (SSPE) were reported in Canada.
- In 1999, only two definite cases of SSPE were confirmed.
- Ongoing attempts to detect and sequence the variant measles virus will be important in order to rule out vaccine-associated SSPE.

"The rarity of SSPE cases is both a tribute to the impact of measles immunization programs, as well as a reassurance about the safety of the measles vaccine.

Dr. Wikke Walop

Background

Subacute sclerosing panencephalitis (SSPE) is a slow-viral infection of the central nervous system following measles infection, usually resulting in death within months or years.[1] The average period between exposure and onset of SSPE ranges from seven to twelve years, while the average age of onset is nine years. SSPE manifests itself as progressive mental deterioration, myoclonia, motor disabilities, coma, and death.[2,3] Both laboratory findings and epidemiological data have linked SSPE with exposure to the wild measles virus.[4]

The incidence of SSPE following measles infection has declined drastically from one per 100,000 cases in the pre-immunization era to 0.06 per 1,000,000 persons since the introduction of immunization programs in the United States.[1,2]

Objective

SSPE is now extremely rare. However, active surveillance for this disease is important to reassure the public about the relative safety of measles immunization, compared with the continued circulation of wild virus and the occurrence of natural infection.

Case definition

For CPSP reporting purposes, only definite cases are considered. All suspect cases should be followed in an attempt to obtain the laboratory information necessary to determine whether it is a definite case.

Definite case

A. High titres of serum antibodies against measles virus and the presence of oligoclonal measles virus antibodies in CSF (serum: CSF measles antibody ratio indicative of intrathecal antibody production)

and/or

B. Measles virus antigen detected in brain tissue by biopsy or at autopsy.

Suspect case

A. Typical clinical history: Usually insidious onset of mental deterioration, followed (usually within a few months) by motor dysfunction, final progressive decerebration and untimely death

and

B. Typical EEG changes (burst-suppression pattern).

Methods

Active surveillance for SSPE is done through the standard CPSP response card sent to participants in Canada. Patients may present initially to any health care provider, but ultimately the diagnosis will be established by a tertiary care provider. Given the long latency from measles virus infection to development of SSPE, some cases may be diagnosed in young adults who may not present to a paediatrician. However, it is hoped that with a diagnosis such as SSPE a paediatrician may become aware of the case and report it.

Duration

January 1997 to December 2000

Results

From 1995 to 1998, no definite cases of SSPE were reported through the CPSP in Canada. In 1999, however, two definite cases, as defined by very high serum and CSF IgG ratios in the presence of typical clinical manifestations, were identified through the CPSP. Both patients were males. One was Canadian-born while the other immigrated to Canada when he was 11 years old. Their ages at diagnosis of SSPE were six and 16 years. The older child has since died, but an autopsy was not performed. The year of onset of symptoms was 1998 and 1996 respectively. The younger Canadian-born child was immunized at age one, while the immunization status of the older foreign-born child could not be confirmed. Both cases had a history of possible early measles infection. One had an undiagnosed rash before immunization, and the other had a history of viral exanthem-like illness around one year of age. Both of these cases were confirmed by serological testing without virus sequencing. Therefore, wild measles virus could have caused both of these cases.

Discussion

Because SSPE is only one of a number of degenerative neurological diseases, it requires a high level of diagnostic suspicion. It is very

important that all suspect cases be followed up with laboratory investigations to determine which are definite cases of SSPE. Serum and CSF measles IgG antibody levels should be determined. Actual titre values are preferred over more general terms, such as positive or negative. With the elimination of indigenous measles disease in Canada, due to widespread measles immunization programs, it is essential that brain tissue specimens be collected post-humously on all suspect cases of SSPE for virus detection.

Brain biopsy material can be examined for measles virus RNA by reverse transcription polymerase chain reaction. Subsequent DNA sequencing of the viral nucleoprotein or hemagglutinin genes allows differentiation of vaccine and wild-type measles strains.[5] In Canada, the Viral Exanthemata Lab at the Bureau of Microbiology performs vaccine versus wild-type strain differentiation for measles, rubella and varicella-zoster viruses.

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1999 Results

Percentage of returned forms

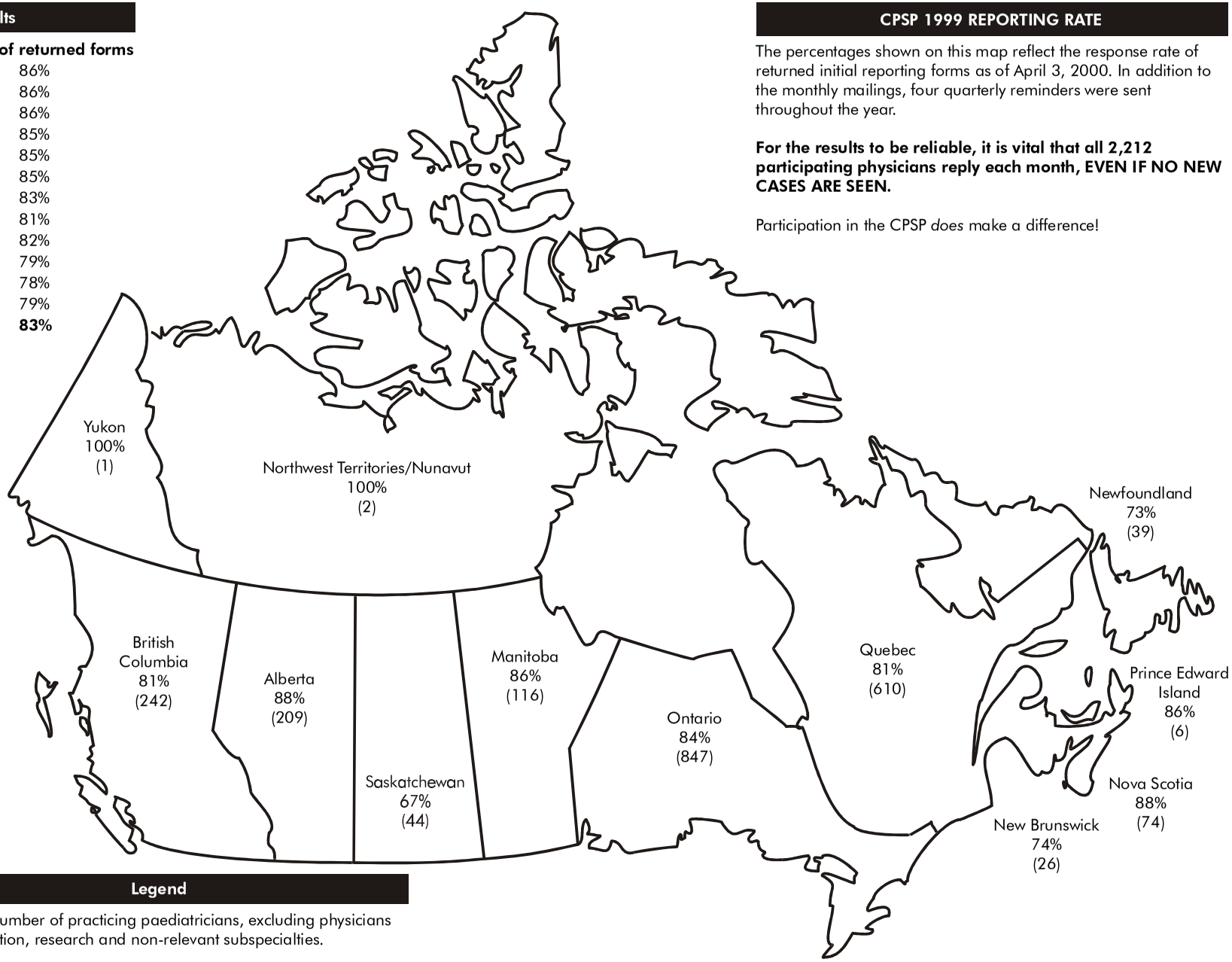
January	86%
February	86%
March	86%
April	85%
May	85%
June	85%
July	83%
August	81%
September	82%
October	79%
November	78%
December	79%
Average	**83%**

CPSP 1999 REPORTING RATE

The percentages shown on this map reflect the response rate of returned initial reporting forms as of April 3, 2000. In addition to the monthly mailings, four quarterly reminders were sent throughout the year.

For the results to be reliable, it is vital that all 2,212 participating physicians reply each month, EVEN IF NO NEW CASES ARE SEEN.

Participation in the CPSP *does* make a difference!



Legend

(xxx) = The number of practicing paediatricians, excluding physicians in administration, research and non-relevant subspecialties.

New Studies in 2000

Anaphylaxis

Dr. Estelle Simons

"Anaphylaxis remains a challenge for diagnosis and treatment.

Anaphylaxis, a severe, acute, potentially fatal allergic reaction, is under-diagnosed and under-treated in children.

By including anaphylaxis in the surveillance program, we hope to improve the chances of survival of children with this disorder by: defining its incidence in Canada, and identifying who experiences it, what triggers it, where it occurs, and how it is managed acutely and in follow-up.

An ideal way to identify paediatric patients with anaphylaxis is through the Canadian Paediatric Surveillance Program, as the physicians involved in this program are key health care providers for Canadian children.

Duration

January 1, 2000 to December 31, 2001

Funding

Anaphylaxis Foundation of Canada, Canadian Allergy, Asthma and Immunology Foundation, and Food Directorate, Heath Canada

Investigators

Estelle Simons*, MD, University of Manitoba
Zave Chad, MD, Ottawa, Ontario
Milton Gold, MD, University of Toronto

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Hemolytic uremic syndrome

"HUS D^+ — HUS remains one of the leading causes of acute renal failure in Canadian children.
Dr. Paul Sockett

HUS D^- — The infrequent form of HUS D^- Streptococcus pneumoniae *associated HUS (SPAH) is linked to a mortality rate* approaching 50%.

Dr. François Proulx

Hemolytic uremic syndrome (HUS) is a heterogeneous condition characterized by microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure. This study aims to determine the incidence of HUS associated with diarrhea (HUS D^+) including verotoxin-producing *Escherichia coli* 0157:H7 (0157:H7 VTEC) and non 0157 strains. HUS D^+, also known as the 'hamburger disease', is a public health problem in many developed countries and remains one of the leading causes of acute renal failure in Canadian children.[1]

Furthermore, this study intends to determine the incidence of invasive *Streptococcus pneumoniae* associated HUS (SPAH), which is an infrequent and particular form of HUS. SPAH is much less well known than VTEC-associated HUS. Nevertheless, it is associated with a significant morbidity and mortality in children. A recent report suggests that the incidence of SPAH is increasing,[2] although distinction with pneumococcal sepsis and secondary organ dysfunction may sometimes be difficult.[3]

The Canadian Paediatric Surveillance Program offers a unique opportunity to conduct these epidemiological studies prospectively and to assure the quality of the data collected. The Bureau of Microbiology, Laboratory Centre for Disease Control, will provide expert support for the microbiological issues. We hope that improving our knowledge of the situation in Canada will lead to appropriate public health action.

References

1. Rowe PC. Consensus statements on behalf of the Canadian Paediatric Kidney Disease Research Centre. *Escherichia coli* 0157:H7, other verotoxin-producing *E. coli*, and hemolytic-uremic syndrome in childhood. Can J Inf Dis 1995;6:105-10.

2. Cabrera GR, Fortenberry J, Warshaw BL, Chambliss CR, Butler JC, Cooperstone BG. Hemolytic uremic syndrome associated with invasive *Streptococcus pneumoniae* infection. Pediatrics 1998;101:699-703.

3. Proulx F, Liet JM, David M, Seidman E, Tapiero B, Robitaille P, Lacroix J. Hemolytic uremic syndrome associated with invasive *Streptococcus pneumoniae* infection. Pediatrics 2000;105:462-3.

Duration

April 1, 2000 to March 31, 2002

Funding

Division of Enteric, Foodborne and Waterborne Diseases, Laboratory Centre for Disease Control, Health Canada

Investigators

For HUS D^+
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For HUS D^-
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Smith-Lemli-Opitz syndrome

"Smith-Lemli-Opitz is an inherited disorder for which we have a diagnostic tool (measurement of plasma 7-DHC level) and a treatment (supplementation of cholesterol). Early identification and treatment of patients with SLO may improve both their general health and behaviour.

Dr. Małgorzata Nowaczyk

Smith-Lemli-Opitz Syndrome (SLO) is an inherited defect of cholesterol synthesis. The enzymatic defect leads to a generalized cholesterol deficiency and to an accumulation of the immediate precursor, 7-dehydrocholesterol

(7-DHC), in all body tissues, resulting in a syndrome of multiple malformations, dysmorphic features, mental retardation, and behavioural abnormalities. SLO is readily diagnosed by demonstration of elevated levels of 7-DHC. Treatment of SLO patients with cholesterol leads to an improvement in their general health and behaviour, and a resultant improvement in their quality of life.

Canada offers a unique opportunity to study this type of rare disease. Key factors in place to facilitate this process include a population that is large enough (~ 30,000,000 people), yet genetically diverse, uniformly excellent tertiary health care facilities, a small group of specialists willing to participate in cooperative nationwide studies, and a successful and a well-established national surveillance program with a high response rate. The main objective of surveillance for SLO is to determine the incidence of SLO in Canada. Based on the annual birth rate in Canada and the current estimates of incidence of SLO (1:20,000 to 1:60,000), seven to 20 new cases of SLO are expected per year.

SLO can be diagnosed easily using well-established, inexpensive methods. If the incidence of SLO is found to be sufficiently high (1:20,000 or higher), then neonatal or prenatal screening may be indicated to reduce the lag time between diagnosing the condition and providing appropriate and timely management of affected patients and their families. Canadian data regarding the incidence of SLO will likely be applicable to estimate the incidence of SLO in other countries with similar ethnic make-up. In addition, information compiled as a result of SLO's inclusion in the surveillance program will be used to facilitate further clinical and basic science studies (e.g., facial anthropometry, effects of dietary therapy, and genotype-phenotype correlation).

Duration

January 1, 2000 to December 31, 2001

Reference

Nowaczyk MJ, Whelan DT, Heshka TW, Hill RE. Smith-Lemli-Opitz syndrome: a treatable inherited error of metabolism causing mental retardation. CMAJ 1999;161(2):165-70.

Funding

Hamilton Health Sciences Foundation

Investigator

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International Developments

Backgound

In August 1998, at the 22nd International Congress of Paediatrics in Amsterdam, ten national paediatric surveillance units met to discuss a proposal that would link pre-existing units and improve international collaboration and discussion. Together, they formed the International Network of Paediatric Surveillance Units (INoPSU). The British Paediatric Surveillance Unit (BPSU), which began in 1986 and has provided a model for establishing similar national surveillance programs in Europe, Asia and Australia, agreed to act as the 'server' of the network. A secretariat, consisting of representatives from the United Kingdom (UK), Australia, Canada and the Netherlands, was set up to carry out the aims and direct the activities of INoPSU.

In addition to the UK and Canada, founding members included units from Australia, Germany, Latvia, Malaysia, Netherlands, New Zealand, Papua New Guinea and Switzerland. More recently, the Welsh unit which was formed in 1995 and concentrates on less rare disorders, became the eleventh unit to join INoPSU. Several countries such as Portugal, Belgium and the Czech Republic have also expressed an interest in developing national paediatric surveillance units.

Mission

The mission of INoPSU is the advancement of knowledge of uncommon childhood infections and disorders through the participation of paediatricians in surveillance on a national and international basis so as to achieve the following aims and benefits:

- to facilitate communication and cooperation between existing national paediatric surveillance units;
- to assist in the development of new units;
- to facilitate sharing information and collaboration between researchers from different nations and scientific disciplines;
- to share information on current, past and anticipated studies and their protocols, and on conditions that have been nominated for surveillance but are not selected;
- to encourage the use of identical protocols to potentially enable simultaneous or sequential collection of data on rare paediatric disorders in two or more countries;
- to share and distribute information of educational benefit to constituent units, notably on study and surveillance methodologies;
- to share statistical techniques and models of evaluation for units;
- to peer review and evaluate existing and proposed units;
- to identify rare disorders of mutual interest and public health importance for cooperative surveys through each national unit;
- to collaborate with, and provide information to, other groups interested in rare childhood diseases, such as parent support groups;
- to respond promptly to international emergencies relating to rare childhood conditions where national and international studies can make a contribution to science or public health.

Developments

For INoPSU to succeed, clearly, a viable network of communication must be in place. To this end,

TABLE 9

National paediatric surveillance units status circa end 1999

Country	Child population (10^6-aged 0-15 years)	Established	Respondents	Response rate
Australia	1.5	1992	934	96%
Britain/Eire	12.8	1986	2005	92%
Canada	6.3	1996	2212	83%
Germany	14.0	1992	468*	94%
Latvia	0.4	1996	22	90%
Malaysia	7.7	1994	395	65%
Netherlands	2.9	1992	432	91%
Papua New Guinea	1.9	1996	40	79%
New Zealand	0.8	1997	165	94%
Switzerland	1.3	1995	40*	99%
Wales	0.6	1995	121	95%

* Heads of Paediatric Centres

TABLE 10

Conditions under surveillance worldwide

Acute flaccid paralysis	Australia, Canada, Netherlands, New Zealand, Papua New Guinea, Switzerland
Anaphylaxis	Canada
Aseptic meningitis following MMR vaccination	Germany
Atresia (stomach, esophagus)	Latvia
Celiac disease	Netherlands
Cerebral edema in diabetic ketoacidosis	Canada
CHARGE association	Australia
Children in house fires	Wales
Congenital adrenal hyperplasia	Netherlands, Wales
Congenital cytomegalovirus infection	Australia
Congenital hypothyroidism	Papua New Guinea
Congenital laryngeal stenosis	Latvia
Congenital nephrosis, Finnish type	Latvia
Congenital rubella	Australia, Britain, Canada, New Zealand, Switzerland
Congenital syphilis	Latvia
Diabetes mellitus	Germany, Netherlands, New Zealand, Papua New Guinea, Wales
Duchenne muscular dystrophy	Malaysia
Encephalitis	Britain

TABLE 10 (continued)

Conditions under surveillance worldwide

Eosinophilic granuloma	Latvia
Fetal alcohol syndrome	New Zealand
GMUT-1 deficiency	Germany
Group B streptococcal infections	Britain, Netherlands
Haemophilus influenzae infections	Australia, Britain, Germany
Hemolytic uremic syndrome	Australia, Britain, New Zealand, Switzerland
Hemorrhagic disease of the newborn (vitamin K deficiency bleeding)	Australia, Canada, Germany, New Zealand, Switzerland
Hirschsprung's disease	Australia
Histiocytosis	Latvia
HIV/AIDS	Australia, Britain, Latvia, Malaysia, Netherlands, New Zealand, Papua New Guinea
Idiopathic and congenital nephrotic syndrome	Australia
Inflammatory bowel disease	Netherlands
Invasive pneumococcal infections	Germany
Ischaemic stroke in infants	Germany
Leukemia (acute lymphoblastic, acute myeloblastic, chronic myeloblastic)	Latvia
Lymphogranulomatosis	Latvia
Malignant disease	Papua New Guinea, Wales
Marfan's syndrome	Wales
Medullary sponge kidney	Latvia
Multiple sclerosis	Germany
Münchausen by proxy syndrome	Australia
Neurologic endemic cretinism	Papua New Guinea
Organoaciduria and fatty acid oxidation defects	Germany
Neonatal herpes simplex	Australia, New Zealand
Neonatal fungal septicemia	Germany
Neural tube defects	Netherlands
Pancreas cystic fibrosis	Latvia
Pertussis	Germany, Netherlands
Pigbel	Papua New Guinea
Polycystic kidney disease	Latvia
Prader-Willi syndrome	Austalia
Primary immunodeficiency disorders	Australia
Progressive intellectual and neurological deterioration/ Creutzfeldt-Jakob disease	Britain, Canada

TABLE 10 (continued)

Conditions under surveillance worldwide

Renal tubular acidosis	Papua New Guinea
Retinopathy of prematurity	New Zealand
Rett syndrome	Australia
Reye's syndrome	Britain
Severe bronchial asthma	Latvia
Severe/fatal allergic reactions to food ingestion	Britain
Severe visual impairment and blindness	Britain
Smith-Lemli-Opitz syndrome	Canada
Subdural haemorrhage	New Zealand, Wales
Tuberculosis	Latvia, Wales
Tracheomalacia	Latvia
Transient myeloproliferative syndrome	Germany
Vitamin C deficiency bleeding	Switzerland
Williams-Campbell syndrome	Latvia

several important developments have occurred over the past few years to assist member units interested in collecting data on similar syndromes across the continents, sharing both good and bad experiences in surveillance, and facilitating the establishment of any new units. More specifically, the Australian Unit prepared a historical paper on the evolution of INoPSU which should be published soon, and the British Unit agreed to act as server for the INoPSU website. Information available on the web includes contact details on member units, summaries of protocols for current, past and anticipated surveys, and a bulletin board for shared discussions.

Attendance at early INoPSU meetings, organized by the British Paediatric Surveillance Unit and held in York and Edinburgh, was somewhat restricted by factors of cost and distance. Thanks to Health Canada for making financial support available to one delegate from each member country, INoPSU 2000 this June in Ottawa will mark the first time that representatives from around the globe will have met to discuss issues and concerns of international paediatric surveillance. By working together to identify some common international studies, INoPSU can make a difference in improving the global health and well-being of our children and youth.

How the CPSP Works

The Canadian Paediatric Surveillance Program provides a surveillance infrastructure to monitor conditions of public health importance that are of such low incidence that national ascertainment of cases is needed. The program provides an active surveillance system in which more than 2,200 paediatricians have been enrolled as participants. Other physicians, such as paediatric neurologists and allergists, are enrolled in the program when research studies indicate their participation. These physicians provide health care to over six million Canadian children and youth.

The Steering Committee selects studies for inclusion in the program through considering the criteria outlined in Table 11.

Study proposals can be submitted at any time through the program coordinator and should follow the format in Table 12. The Steering Committee reviews submissions at its spring meeting, giving preference to studies that have their own funding source. Individual researchers are encouraged to make early contact with the CPSP Coordinator to discuss the appropriateness of the program for collecting the data, to define the costs, and to identify possible funding agencies. Although the program was initiated with full funding from Health Canada, it is expected that Health Canada will reduce its funding to include only the program's core activities with individual researchers providing sufficient funds to cover the CPSP's 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. The current cost to researchers who wish to use the CPSP services is $22,000 for the first year and $18,000 for each subsequent year. Studies must be submitted to an Ethical Review Board for approval before receiving final acceptance to the program.

TABLE 11

Criteria for inclusion of studies

Rarity	Disorders of such low incidence or prevalence that national ascertainment of cases is needed (less than 1,000 cases a year).
Public health importance	Clearly addressing a public or paediatric health issue.
Scientific importance	Demonstrated scientific interest and importance.
Uniqueness	Proposal must demonstrate a clear need for data on a condition or disorder for which there is only limited information and for which surveillance is the most appropriate means of collecting the data.
Quality of proposal	Proposal must state clear and achievable objectives, practicability, patient confidentiality, adequate 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 under-notification. Investigators are expected to demonstrate that potential funding is available.

TABLE 12

Format for submission

Proposals for new studies should include:

- 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
- identification of projected date for completion of analysis and submission for publication

Reporting methodology

The CPSP uses a two-tiered reporting process to ascertain and investigate cases: an initial 'check-off' form and a detailed report form. The initial report form, listing the conditions currently under surveillance, is mailed monthly to all practising Canadian paediatric health care providers. Respondents are asked to indicate, against each condition, the number of new cases seen in the last month, including nil reports. Each respondent returns the form to the CPSP office in a postage-paid envelope. While non-nominal patient information, such as the date of birth and sex of the child, as well as comments on the condition are requested for each reported case, the CPSP assures the confidentiality of all information provided to the program. This information is used to identify duplicates and is entered, as a reminder, on a detailed report form, which 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. The investigator is responsible for contacting the respondent if further information is required.

The detailed report forms are developed by the investigator and must receive Steering Committee and ethical approval before use. For each study initiated through the CPSP, program participants receive a summary of the protocol, including the case definition and brief description of the condition. 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. These reminders have significantly improved response rates and the ascertainment of cases. To keep participants informed of progress, monthly compliance rates and case reports are mailed quarterly to all participants.

A current mailing list of participants is regularly updated to reflect considerable changes, including new certificants and recent retirees. The main challenge is to ensure that participants in the database are actively practising in Canada, since reporting rates depend on the accuracy of this list. Participants are also encouraged to report all cases meeting the case definitions that come to their attention. The CPSP needs to hear back from **all** participants, whether they have seen a new case or not. Even a 'nothing to report' response is vital in assuring completeness of case ascertainment by helping the CPSP reach its goal of 90% response. This sometimes leads to duplicate reports but avoids missed cases. Duplicates are identified during case follow-up.

Investigators provide an annual report on progress for the Steering Committee and for 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.

(Adapted from PN Sockett, Canadian Paediatric Surveillance Program: Two years of a system for investigating unusual paediatric disorders. Paediatr Child Health 1998;3:241-2, by permission of Pulsus Group Inc.)

TABLE 13

Summary of services provided by CPSP to researchers

- ✔ High case ascertainment: goal of over 90% response from more than 2,200 participants
- ✔ Very inexpensive means of identifying and obtaining data on rare diseases and conditions
- ✔ Active surveillance: participants complete the check-off form each month, indicating new cases or 'nothing to report'
- ✔ Timely surveillance: a mail-out each month to all participants
- ✔ All administrative services
- ✔ High response rate: follow-up reminders to participants who have not responded
- ✔ Timely feedback of results to participants: quarterly summary reports
- ✔ Full-time program coordinator
- ✔ Access to a CPSP consultant (Medical Affairs Officer)
- ✔ Full vetting of research proposals by the CPSP Steering Committee
- ✔ Annual surveillance summaries, authored by each researcher, published in the *CPSP Results*
- ✔ Presentation of surveillance summary/results at the Steering Committee meetings – opportunity for discussion
- ✔ Opportunity for international collaboration with other paediatric surveillance units worldwide
- ✔ The chance to make a difference in the health and well-being of Canadian children and youth
- ✔ Increased awareness of rare paediatric conditions among the health care community
- ✔ Existence of an effective surveillance system, should a new public health issue arise

Notes


CPSP