CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM

2000 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:

Canadian Paediatric Society

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Acknowledgements

It takes many players to succeed in any project. This 2000 annual report of the Canadian Paediatric Surveillance Program (CPSP) highlights the many contributions that have resulted in our program's success.

The key to the CPSP's strength is the participation of Canadian paediatricians, subspecialists and other health-care providers in the monthly collection of information on rare paediatric conditions. These are our most valued players.

Also highly valued are our principal investigators who review and analyze the data collected to provide us with knowledge and educational solutions to help children and youth around the world.

The Canadian Association of Paediatric Hospitals, IMPACT (Immunization Monitoring Program ACTive) centres, Notifiable Diseases Reporting System and CJD-Surveillance System Canada deserve a special thank you for their role in the verification of data collected. Our continued association can only bring more credibility to our case ascertainment.

A sincere thank you goes to the CPSP Steering Committee members. These are the coaches who continue to guide the program by providing a wealth of knowledge and leadership while addressing key challenges for the future.

Of course a program such as this one cannot function without funding, a summary of which is found in this report. We gratefully acknowledge the financial support from all our funders.

In closing, we highlight the CPSP partnership between the Canadian Paediatric Society (CPS) and Health Canada's Centre for Infectious Disease Prevention and Control (CIDPC). This is not a partnership in name only. The CPS administers the program with very strong intellectual as well as financial support from the CIDPC. CIDPC's participation and commitment have enabled the program to grow and disseminate valuable information on uncommon paediatric diseases and conditions.

Message from the Minister of Health

As Minister of Health, I commend the Canadian Paediatric Surveillance Program (CPSP) on its achievements over the past five years. The Program's success is due, in large part, to the commitment of the paediatricians, geneticists, allergists and other health-care workers who diligently complete and return the monthly 'report card'. As well, the Canadian Paediatric Society must be recognized for its vital role in the day-to-day operation of the CPSP.

An essential aspect of the Program is the ability to link information obtained by health-care workers who provide care and treatment to children with rare conditions to those who can use the information to improve the lives of children and youth.

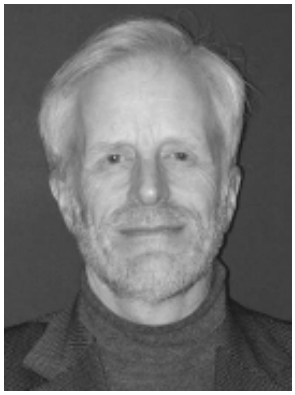
I congratulate the CPSP on its role in the successful initial meeting of the International Network of Paediatric Surveillance Units held in Ottawa in June 2000. The Network provides a unique mechanism for international collaboration by providing a rich backdrop of diverse geographical locations and population characteristics.

This year's Speech from the Throne recognized the importance of children and families. Securing a good start in life for children is the only way to ensure that they are ready to learn, to seize opportunity as adults, and to contribute to the building of their country.

The CPSP is an important step to ensuring a good start in life for our children and youth. On behalf of all Canadians, I wish the Program continued success.

Allan Rock
Minister
Health Canada

Message from the Director General, Centre for Infectious Disease Prevention and Control



I am pleased to accept the fifth annual report of the Canadian Paediatric Surveillance Program (CPSP). This program, designed to monitor and contribute to the improvement of health of all Canadian children and youth, has resulted in an increased knowledge of uncommon childhood conditions and the practical improvement in prevention and treatment.

The surveillance of vaccine-preventable diseases continues to be a particular focus of the program. Canada is a global partner in the World Health Organization's polio eradication initiative. Until every region in the world is certified polio-free and global eradication is attained, there is a risk of wild poliovirus importation from polio-endemic regions to Canada. Consequently, Canada remains committed to the monitoring of its polio-free status through the CPSP by surveillance of acute flaccid paralysis. Canada is also committed to monitoring the effectiveness of the measles-mumps-rubella immunization program through the CPSP's surveillance of congenital rubella and subacute sclerosing panencephalitis. Since 1970, the incidence of rubella in Canada has declined markedly; however, there are still reported cases.

I would like to thank the staff of the Centre for Infectious Disease Prevention and Control (CIDPC) who form the foundation of the partnership with the Canadian Paediatric Society in the administration of the program. CIDPC is committed to the continuation of the partnership as it builds on the success of the past five years in facilitating communication, cooperation and collaboration among diverse professional disciplines in many nations working toward the well-being of children.

I am gratified by the success of the first formal meeting of the International Network of Paediatric Surveillance Units that was hosted by the CPSP in Ottawa in June 2000. International collaboration on surveillance and research is becoming increasingly important as the movement of people across the globe becomes commonplace.

I wish to thank the participants, the paediatricians, the allergists, the neurologists, the geneticists and the intensivists, for their dedication to the program. The success of active surveillance is due to the large number of participants who return the monthly reporting form.

A healthy Canadian society is built on the health and well-being of individual Canadians and the health of our communities. Programs, such as the CPSP, provide the building blocks for the health of our children, youth and their families, and of our future generations.

Paul Gully
A/Director General
Centre for Infectious Disease Prevention and Control

Message from the President of the Canadian Paediatric Society

For the past five years, Canadian paediatricians, paediatric subspecialists and health-care providers have actively participated in surveillance of rare diseases and conditions of public health importance through the Canadian Paediatric Surveillance Program (CPSP), a partnership program between the Canadian Paediatric Society (CPS) and Health Canada's Centre for Infectious Disease Prevention and Control.

There are many important reasons why we participate in this program. Timely epidemiological prospective data collection has a direct impact on the diagnosis and treatment of patients. Surveillance of rare genetic conditions may identify populations at risk, which, in turn, may lead to implementation of population-based screening programs. Such programs allow for intervention at younger ages, thereby improving quality of life. Data collection can monitor the incidence of disease before vaccination as well as the effectiveness of immunization programs.

Hemorrhagic disease of the newborn study results have supported the Canadian Paediatric Society's guidelines on the administration of intramuscular vitamin K to newborn babies. Increased awareness and earlier diagnosis of a treatable inherited disease such as Smith-Lemli-Opitz syndrome, will improve the general health, behaviour and quality of life of affected patients and their families. The rarity of subacute sclerosing panencephalitis (SSPE) cases (two in four years) is both a tribute to the success of the measles immunization program, as well as reassurance about the safety of the measles vaccine.

The CPSP is also a valuable educational resource. Study protocols and associated educational articles offer a great way to acquire Maintenance of Certification credits. Under the Royal College of Physicians and Surgeons of Canada (RCPSC) classification entitled "Structured learning projects" (Section 4), physicians can earn one credit per hour, with no maximum when they document the question, its source, references and the practical outcome of learning.

Moreover, specific resource articles are developed and distributed, where appropriate, such as the article on the treatment of cerebral edema in diabetic ketoacidosis, for posting in paediatric and community hospital emergency rooms to improve recognition and management. The first CPSP highlight on the value of collecting stool cultures for surveillance of acute flaccid paralysis was published in the November/December issue of *Paediatrics & Child Health*. CPSP highlights will become a monthly feature in 2001. Pan-Canadian analysis and summary data is published in the annual CPSP Results and upon completion of a study in peer-reviewed journals and at scientific meetings. The list of CPSP publications and presentations is growing (see pages 7-8).

We, at the CPS, firmly believe that our continued diligent participation in our national surveillance system will bring further knowledge and educational solutions that will benefit children and youth around the world. Thank you for your support of this important program.

David F. Smith, MD, FRCPC
President, Canadian Paediatric Society

CPSP Chairman's Report

On this fifth anniversary, the CPSP is getting closer to its ascertainment response rate goal of 90%. The CPSP Working Group and Steering Committee are committed to developing new ways of sharing information to showcase the value of active surveillance and keep participants interested and engaged in the program. As a result, we can now lay claim to an impressive 95% response rate for detailed case reporting, a truly impressive achievement in light of the nearly 830 cases reported. Participants are strongly encouraged to report all known cases, even if they suspect they may be duplicates. Case ascertainment is monitored and verified by investigating duplicate reports and comparing data with other existing programs and centres. Duplication of case reports is both expected and valued.

With increased concerns about the protection of individual privacy, an important issue for paediatric surveillance becomes the need to balance the goal of data collection for the common good against the need for confidentiality. The CPSP is committed to maintaining patient confidentiality. Only non-nominal patient information, such as the date of birth and sex of the child, as well as comments on the condition, is requested for each reported case. This information is used to identify duplicates and serve as a reminder on the detailed report form to request case-specific information.

At the most recent Steering Committee meeting, Mr. Paul Muirhead, a lawyer with specialization in biomedical ethics, and Dr. Michael Yeo, Ethicist of the Canadian Medical Association and Adjunct Professor at the University of Ottawa, led an ethics workshop where various ethical issues were discussed. While health-related surveillance has existed for centuries, the difference today is the rapidly increasing technological ability to link, analyze and spread data. The CPSP renewed its commitment to ensuring the privacy and the non-labelling of individuals, localities, and provinces involved in either rare encounters of a condition or localized outbreaks. Only pan-national data is used in presentations and publication of study results.

Being a member of the International Network of Paediatric Surveillance Units (INoPSU) provides remarkable opportunities for international collaboration and data comparison. One CPSP study likely to come on stream in 2001 is CHARGE association/syndrome (CAS). Children with CAS have variable combinations of abnormalities, including coloboma, choanal atresia and cardiac, renal, genital and gastrointestinal abnormalities. As this condition is currently under study in Australia, the CPSP anticipates a valuable exchange of knowledge in the foreseeable future.

I urge you to read this year's study results. The successes, achieved by your participation and support of the CPSP, speak for themselves. Our challenge for 2001 will be to reach a response rate of 90% for both initial and detailed reporting.

A sincere 'thank you' to those who have worked so hard to establish and promote this active surveillance program. The past five years have resulted in considerable support and acceptance. Participation of a dedicated paediatric community, the guidance of the Steering Committee, the exceptional efforts of the Working Group and support of Health Canada's Centre for Infectious Disease Prevention and Control have made a bright future possible.

Richard Stanwick, MD, FRCPC
Chairman
CPSP Steering Committee

CPSP Steering Committee 2000

Dr. Richard Stanwick	Chairman
Dr. Ronald Barr	Canadian Paediatric Society
Ms. Marie Adèle Davis	Canadian Paediatric Society
Dr. Gilles Delage	Canadian Paediatric Society
Ms. Jo-Anne Doherty	Centre for Infectious Disease Prevention and Control, Health Canada
Dr. Monique Douville-Fradet	Advisory Committee on Epidemiology
Dr. Frank Friesen	Canadian Paediatric Society
Dr. Danielle Grenier	Medical Affairs Officer
Dr. Richard Haber	Canadian Paediatric Society
Dr. Jack Holland	Assembly of Canadian University Paediatric Department Heads
Dr. Miriam Kaufman	Canadian Paediatric Society
Dr. Daniel Keene	Liaison, Canadian Association of Child Neurology
Dr. Arlene King	Centre for Infectious Disease Prevention and Control, Health Canada
Dr. Catherine McCourt	Centre for Healthy Human Development, Health Canada
Dr. Victor Marchessault	Honourary member
Ms. Andrea Medaglia	Program Coordinator
Dr. Angus Nicoll	Liaison, British Paediatric Surveillance Unit
Dr. Jeff Scott	Council of Chief Medical Officers of Health
Dr. Paul Sockett	Consultant
Dr. Anne Summers	Liaison, Canadian College of Medical Geneticists
Dr. John Waters	Canadian Paediatric Society
Dr. John Watts	Canadian Paediatric Society

CPSP Working Group

Ms. Andrea Medaglia	CPSP Coordinator (Chair), Canadian Paediatric Society
Ms. Marie Adèle Davis	Executive Director, Canadian Paediatric Society
Ms. Jo-Anne Doherty	Chief, Division of Disease Surveillance, Centre for Infectious Disease Prevention and Control, Health Canada
Dr. Danielle Grenier	CPSP Medical Affairs Officer, Canadian Paediatric Society

Publications

Published papers related to studies

Protocol for the investigation of acute flaccid paralysis and suspected paralytic poliomyelitis. Working Group on Polio Eradication, Bentsi-Enchill A. Paediatr Child Health 1997; 2: 409-12

Approach to the bleeding newborn. McMillan DD, Wu J. Paediatr Child Health 1998; 3: 399-401

The Canadian Paediatric Surveillance Program: Two years of a system for investigating unusual paediatric disorders. Sockett PN. Paediatr Child Health 1998; 3: 240-5

Following up on unfinished business – Prenatal rubella screening and postpartum vaccination. Tam T. CMAJ 1998; 159: 117-8

Prevention of congenital rubella syndrome. Canadian Paediatric Society Infectious Diseases and Immunization Committee. Paediatr Child Health 1999; 4: 155-7

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

LCDC Report: Establishing priorities for national communicable disease surveillance. National Advisory Committee on Epidemiology Subcommittee. Doherty J. Can J Infect Dis 2000; 11: 21-2

Epinephrine for outpatient treatment of anaphylaxis (EFOTA): A population-based study. Black CD, Peterson S, Simons FER. J Allergy Clin Immunol 2001; 107: S59

DHCR7 genotypes of cousins with Smith-Lemli-Opitz syndrome. Nowaczyk MJM, Heshka TW, Eng B, Feigenbaum AJ, Waye JS. Am J Med Genet 2001; 100: 162-3

EpiPen Jr and EpiPen dispensing patterns for children – A population-based study. Black CD, Peterson S, Simons FER. Ann Allergy Asthma Immunol 2001; 86: (in press)

Incidence of Smith-Lemli-Opitz syndrome in Ontario, Canada. Nowaczyk MJM, McCaughey D, Whelan DT, Porter FD. Am J Med Genet (in press)

The Smith-Lemli-Opitz syndrome: A novel metabolic way of understanding developmental biology, embryogenesis, and dysmorphology. Nowaczyk MJM, Waye JS. Clin Genet (in press)

Rapid molecular prenatal diagnosis of Smith-Lemli-Opitz syndrome. Nowaczyk MJM, Garcia DM, Eng B, Waye JS. Am J Med Genet (in press)

Smith-Lemli-Opitz syndrome: Holoprosencephaly and IVS8-1G→C/IVS8-1G→C genotype. Nowaczyk MJM, Farrell SA, Sirkin WL, Velsher L, Krakowiak PA, Waye JS, Porter FD. Am J Med Genet (in press)

Highlights published in *Paediatrics & Child Health*

Don't 'pooh-pooh' stool cultures for surveillance of acute flaccid paralysis. Paediatr Child Health 2000; 8: 454

Presentations

Reports of hemorrhagic disease of the newborn (HDNB) to the Canadian Paediatric Surveillance Program (CPSP): Frequency, errors and relationship to vitamin K. McMillan DD, Wu J. Paediatr Child Health 2000; Suppl A: 14A. Abstract presented at the Canadian Paediatric Society's conference *Beyond 2000: Healthy Tomorrows for Children and Youth*, June 14-18, 2000.

Progressive intellectual and neurological deterioration in paediatric population (PIND). Keene D, Sutcliffe T, and Canadian Paediatric Surveillance Program. Paediatr Child Health 2000; Suppl A: 16A. Abstract presented at the Canadian Paediatric Society's conference *Beyond 2000: Healthy Tomorrows for Children and Youth*, June 14-18, 2000, and at the Canadian College of Neurologists' Ottawa meeting in June 2000.

Funding

Funding for the Canadian Paediatric Surveillance Program (CPSP) is divided into two categories: core funding and study funding.

Core funding

Core funding covers administrative costs pertaining to the program including the salary of a full-time program coordinator, a part-time administrative assistant, as well as part salaries for administrative and financial support. The Centre for Infectious Disease Prevention and Control, Health Canada, provides this core funding.

Study funding

The CPSP provides researchers with a very inexpensive, timely and effective means of first identifying and then obtaining follow-up data on rare conditions and diseases.

Researchers and 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 (see Table 3, page 13). While researchers are expected to obtain funding for their studies, the CPSP is more than willing to work with individual researchers to secure funding.

Funding Sources

The CPSP gratefully acknowledges funding for studies in 2000 from the following:

Government departments, Health Canada:

• Acute flaccid paralysis	CIDPC, Population & Public Health Branch
• Anaphylaxis	Food Directorate, Health Products and Food Branch
• Congenital rubella syndrome	CIDPC, Population & Public Health Branch
• Hemolytic uremic syndrome	CIDPC, Population & Public Health Branch
• Hemorrhagic disease of the newborn	CIDPC, Population & Public Health Branch
• Neonatal herpes simplex virus infection	CIDPC, Population & Public Health Branch
• Progressive intellectual and neurological deterioration	CIDPC, Population & Public Health Branch
• Subacute sclerosing panencephalitis	CIDPC, Population & Public Health Branch

CIDPC = Centre for Infectious Disease Prevention and Control

Non-governmental sources:

Anaphylaxis

ANAPHYLAXIS FOUNDATION OF CANADA

Canadian Allergy, Asthma and Immunology Foundation

Cerebral edema in diabetic ketoacidosis

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

Smith-Lemli-Opitz syndrome

HAMILTON HEALTH FOUNDATION

How the CPSP Works

The difficulty in recognizing rare disease can result in delayed diagnosis, increasing the risk of preventable complications or death. Emerging infections will initially be rare and may remain undetected allowing infection to spread extensively before action is taken. All such diseases are difficult to study as their low frequency often means that little may be known about their etiology, clinical spectrum, sequelae, pathological features, diagnosis, treatment and management. Data collection from a large and often geographically diverse population is required to generate a sufficient number of cases to derive meaningful data.

The Canadian Paediatric Surveillance Program was instituted to enable the collection of national epidemiological data in the study of rare diseases of Canadian children and youth. More than 2,300 paediatricians have been enrolled as participants in this active surveillance system. Other participants, such as paediatric neurologists, allergists, medical geneticists and intensivists are enrolled in the program when research studies indicate their participation. These physicians provide health care to over six million Canadian children and youth.

Selection of studies

The Steering Committee selects studies for inclusion in the program through considering the criteria outlined in Table 1.

Study proposals can be submitted at any time through the Program Coordinator and should follow the format in Table 2. The Steering Committee reviews submissions at its spring and fall meetings, giving preference to studies that have either strong public health importance or could not be undertaken any other way, and for which a funding source is clearly identified. Individual researchers are encouraged to make early contact with the Program Coordinator to

TABLE 1

Criteria considered for inclusion of studies

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

Priority will be given to diseases that are not currently notifiable or, if notifiable, have sufficient indication of under-notification. Investigators are expected to demonstrate that potential funding is available.

TABLE 2

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

discuss the appropriateness of the program for collecting the data, to define the costs, and to identify possible funding agencies. See Table 3 for a summary of services provided. The CPSP is willing to provide limited help in obtaining funds, and assistance in coordinating arrangements for funding. Studies must be submitted to an ethical review board for approval before receiving final acceptance to the program.

Reporting methodology

The CPSP uses a two-tiered reporting process to ascertain and investigate cases: an initial 'check-off' form and a detailed reporting form. The full process is summarized in Figure 1.

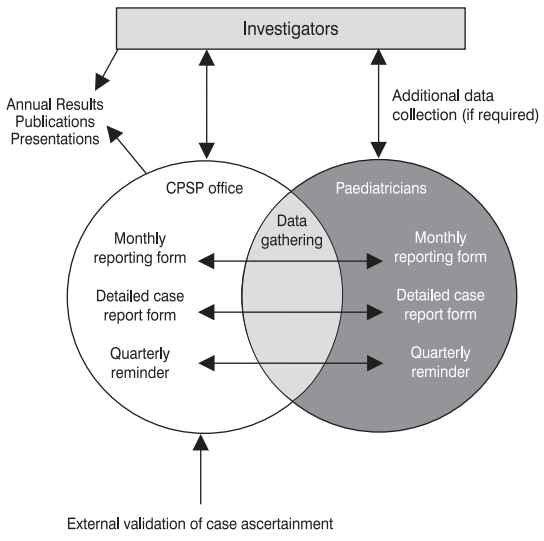
Initial reporting

The initial reporting form (Figure 2), listing the conditions currently under surveillance, is mailed monthly to practising Canadian paediatricians and relevant paediatric subspecialists and health-care providers. Respondents are asked to indicate, against each condition, the number of new cases seen in the last month, including nil reports, as the CPSP cannot simply assume that no reply means no cases. Forms are returned to the CPSP office in a postage-paid envelope.

Participants are encouraged to report all cases meeting the case definitions that come to their attention. If in doubt about whether or not to report, it is best to do so. This sometimes leads to duplicate reports but avoids missed cases. Duplicates are identified during case follow-up. 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

FIGURE 1

Reporting process summary

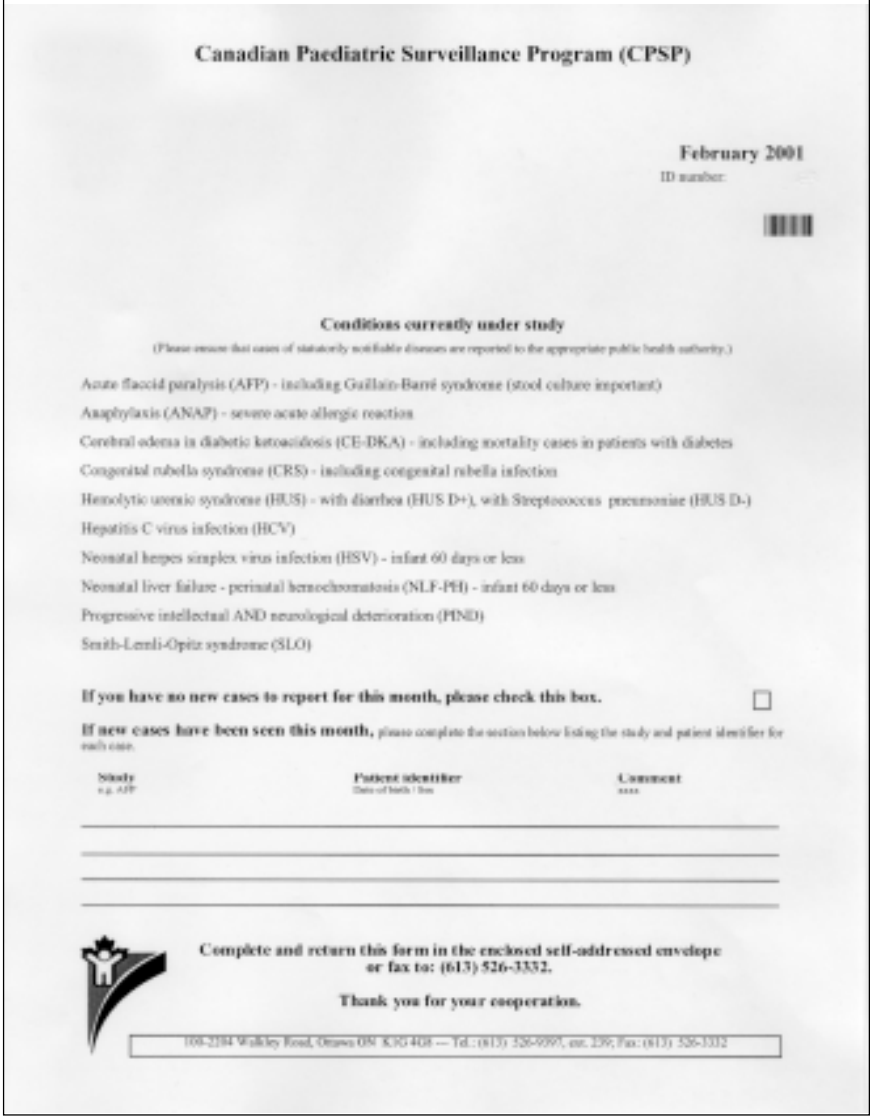


helping the CPSP reach its goal of 90% response.

Quarterly reminders are mailed to respondents who have not replied for all months of the year. These reminders have greatly improved response rates and the ascertainment of cases. To keep participants informed of progress, monthly compliance rates and the number of cases reported are mailed quarterly to all participants.

FIGURE 2

Current CPSP monthly reporting form



Canadian Paediatric Surveillance Program (CPSP)

February 2001

ID number:

Conditions currently under study

(Please ensure that cases of statutorily notifiable diseases are reported to the appropriate public health authority.)

Acute flaccid paralysis (AFP) - including Guillain-Barré syndrome (stool culture important)

Anaphylaxis (ANAP) - severe acute allergic reaction

Cerebral edema in diabetic ketoacidosis (CE-DKA) - including mortality cases in patients with diabetes

Congenital rubella syndrome (CRS) - including congenital rubella infection

Hemolytic uremic syndrome (HUS) - with diarrhea (HUS D+), with Streptococcus pneumoniae (HUS D-)

Hepatitis C virus infection (HCV)

Neonatal herpes simplex virus infection (HSV) - infant 60 days or less

Neonatal liver failure - perinatal hemochromatosis (NLF-PH) - infant 60 days or less

Progressive intellectual AND neurological deterioration (PIND)

Smith-Lemli-Opitz syndrome (SLO)

If you have no new cases to report for this month, please check this box. ☐

If new cases have been seen this month, please complete the section below listing the study and patient identifier for each case.

Study (e.g. AFP) | Patient identifier (Date of birth / Sex) | Comment (xxxx)

Complete and return this form in the enclosed self-addressed envelope or fax to: (613) 526-3332.

Thank you for your cooperation.

[redacted]

Follow-up and confirmation of case reports

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 educate and increase awareness of unusual or rare conditions.

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.

Validation of case ascertainment

Multiple checks and balances are in place to confirm the overall quality and reliability of CPSP data. Case ascertainment is monitored and verified by investigating duplicate reports and comparing data with the following programs/centres:

- Canadian Association of Paediatric Hospitals medical records ICD coding
- IMPACT (Immunization Monitoring Program ACTive) centres
- Notifiable Diseases Reporting System
- CJD-Surveillance System Canada
- Canadian Institute for Health Information

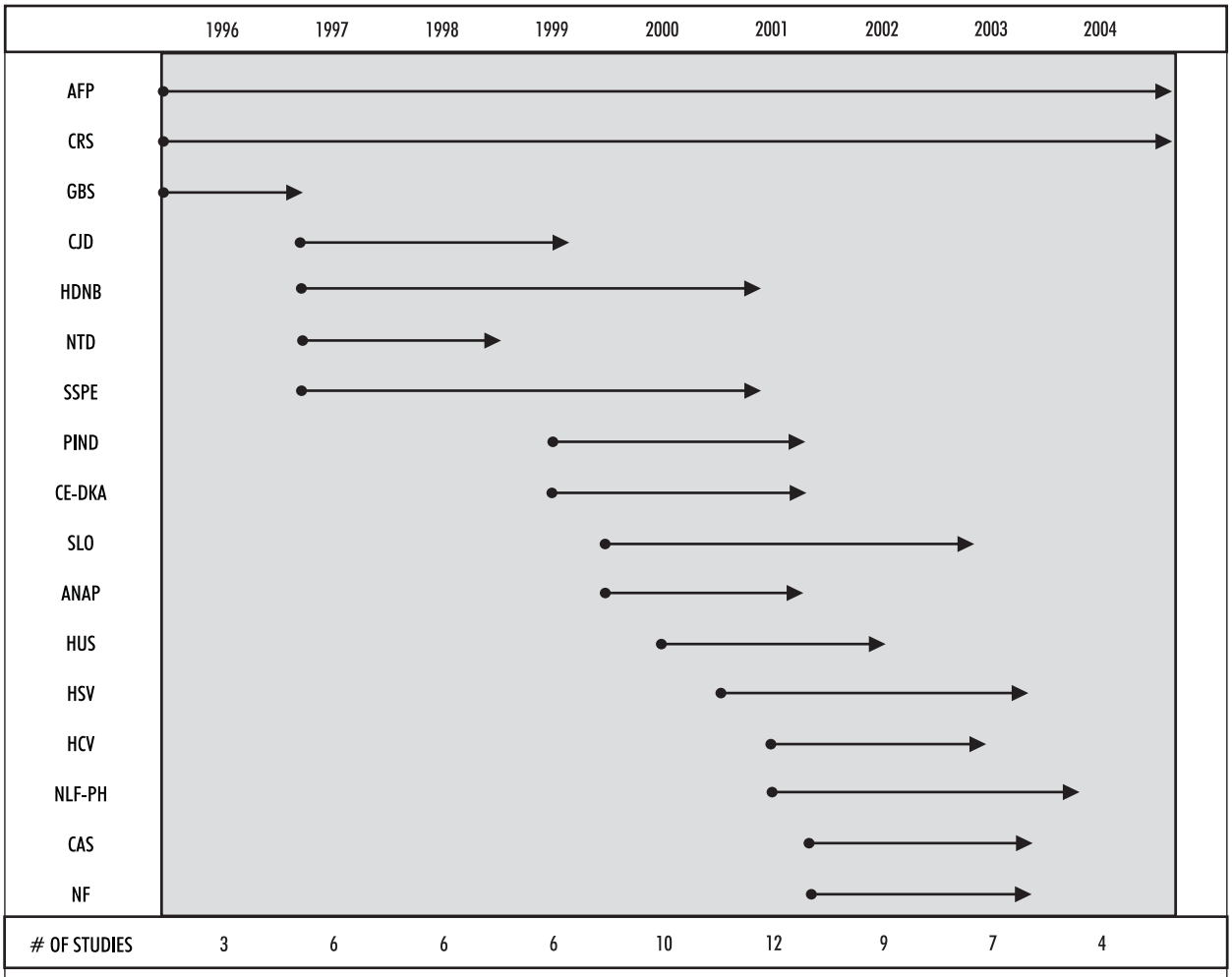
To ensure completeness of case ascertainment so that investigators can capture the data necessary for proper analysis, the CPSP has set a goal of 90% participant response.

TABLE 3

Summary of services provided by the CPSP to researchers

- ✔ High case ascertainment: goal of over 90% response from more than 2,300 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

CPSP At-A-Glance Studies Timeline



AFP = Acute flaccid paralysis: Jan 1996 to Dec 2004
CRS = Congenital rubella syndrome: Jan 1996 to Dec 2004
GBS = Group B strep: Jan 1996 to Dec 1996
CJD = Creutzfeldt-Jakob disease: Jan 1997 to Jun 1999
HDNB = Hemorrhagic disease of the newborn: Jan 1997 to Dec 2000
NTD = Neural tube defects: Jan 1997 to Dec 1998
SSPE = Subacute sclerosing panencephalitis: Jan 1997 to Dec 2000
PIND = Progressive intellectual and neurological deterioration: Jul 1999 to Jun 2001
CE-DKA = Cerebral edema in diabetic ketoacidosis: Jul 1999 to Jun 2001
SLO = Smith-Lemli-Opitz syndrome: Jan 2000 to Dec 2002
ANAP = Anaphylaxis: Jan 2000 to Jun 2001
HUS = Hemolytic uremic syndrome: Apr 2000 to Mar 2002
HSV = Herpes simplex virus: Oct 2000 to Sep 2003
HCV= Hepatitis C virus infection: Feb 2001 to Jan 2003
NLF-PH = Neonatal liver failure/Perinatal hemochromatosis: Feb 2001 to Jan 2004
CAS = CHARGE association/syndrome: Fall 2001 to fall 2003
NF = Necrotizing fasciitis: Fall 2001 to fall 2003

Surveillance Studies in 2000

Acute flaccid paralysis

Highlights

- No cases of polio have been identified in Canada since the start of acute flaccid paralysis surveillance in 1996.
- 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 2000, as in the previous year, the AFP study met the internationally targeted rate of one AFP case per 100,000 children under 15 years of age expected to occur in the absence of wild polio.

"Canada continues to contribute to the better understanding of the neuropathological manifestations of AFP in children in a polio-free environment.

Dr. Paul Varughese

Summary

Fifty-seven confirmed acute flaccid paralysis (AFP) cases, with a mean age of six years, were reported to the CPSP in 2000; the rate (0.97 per 100,000) is almost 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 2000 represents a 32.5% increase over the number of cases reported for 1998, but is 3% less than in 1999. As in previous years, the majority (46 cases or 80.7%) of cases were diagnosed as Guillain-Barré syndrome (GBS), followed by transverse myelitis (4 cases or 7.0%).

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 old 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 59 cases per year. AFP surveillance in Canada was initiated in 1991 through the 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 2000 and compares them to those from previous years.

Objective

The objective of AFP surveillance is to identify AFP cases (including GBS) 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.

TABLE 4

Age distribution of AFP cases reported to the CPSP, 1996-2000

Age group (years)	Number of cases (%)				
	1996	1997	1998*	1999†	2000
0 – 1	2 (6.7)	—	2 (4.6)	3 (4.9)	2 (3.5)
2 – 5	11 (36.7)	13 (37.1)	15 (34.9)	18 (29.5)	23 (40.4)
6 – 10	9 (30.0)	12 (34.3)	18 (41.9)	23 (37.7)	20 (35.1)
11 – <15	8 (26.6)	10 (28.6)	8 (18.6)	17 (27.9)	12 (21.0)
Total	**30 (100)**	**35 (100)**	**43 (100)**	**61 (100)**	**57 (100)**

* Based on cases with age specified

† Includes two delayed reports not included in the *CPSP 1999 Results*

TABLE 5

Neurological diagnosis of AFP cases reported to the CPSP, 1996-2000

Final Diagnosis	Number of cases (%)				
	1996	1997	1998	1999*	2000
Polio	0	0	0	0	0
Guillain-Barré syndrome	21 (70.0)	29 (82.8)	34 (77.3)	50 (82.0)	46 (80.7)
Transverse myelitis	6 (20.0)	2 (5.7)	6 (13.6)	7 (11.5)	4 (7.0)
Encephalitis/encephalomyelitis/encephalopathy	1 (3.3)	1 (2.9)	1 (2.3)	—	—
Myelopathy	—	1 (2.9)	—	—	—
Radiculopathy/radiculoneuritis	1 (3.3)	1 (2.9)	—	—	—
Plexitis/lumbosacral plexitis	—	—	—	2 (3.3)	—
Brachial neuritis	—	—	—	1 (1.6)	—
Rhombomyelitis	—	—	—	1 (1.6)	—
Other	—	—	—	—	7 (12.3)
Not specified/undetermined diagnosis or etiology	1 (3.3)	1 (2.9)	3 (6.8)	—	—
Total	**30 (100)**	**35 (100)**	**44 (100)**	**61 (100)**	**57 (100)**

* Includes two delayed reports not included in the *CPSP 1999 Results*

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. Case-specific information is reviewed by Health Canada's study investigator and cases compatible with the suspected paralytic poliomyelitis case definition

are referred to the National Working Group on Polio Eradication for further review.[2]

Results

In 2000, the CPSP received 97 initial AFP reports, of which 40 (41.2%) were discarded. They included 38 duplicate reports and two cases that did not meet the AFP surveillance case definition, because the patients were 15 years of age or older.

Of the remaining 57 confirmed AFP cases, 41 (71.9%) were males and 16 (28.1%) were females. The cases ranged in age from five months to 14.3 years (median 5.4, mean 6.0 years). Table 4 shows the age distribution of AFP cases reported in 2000 compared with cases reported from 1996 to 1999. Overall, the age distribution is similar throughout the reporting period.

Polio vaccination status: In 2000, only 40 cases (70%) had documentation for having received any polio vaccination; for the remaining 17 cases, no polio vaccine-specific information was available on the case report form. Of these 40 cases assessed, 34 (85%) had received age-appropriate polio immunization.

Virological investigation for polio or other enteroviruses: A total of 29 (50.9%) cases had stool examination; virology was not done or the status was unknown for 28 (49.1%) cases. However, 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 only for 26 (45.6% of 57) cases (for three additional cases, although stool specimens were collected, it was after two weeks of onset of paralysis); none were positive for polioviruses, but one had 'enterovirus' and one had 'echoviruses'. None of the nine throat and/or cerebrospinal fluid specimens collected for viral isolation was positive for poliovirus.

For three cases, serological investigations were done: for one case, paired serological tests for polio-specific antibody titres were performed, but were negative for poliovirus infection (titres less than 1:10); for the second case, only a single titre was done, but the result was inconclusive (titre less than 1:10), and for the third case, the result was not available.

Neurological investigations consisted of at least one of the following: 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 43 (75.4%) cases. Electromyography and/or nerve conduction studies were done for 40 cases; 36 (90%) of these cases had abnormal findings. For 31 cases in which MRI or CT scanning was done, 10 were reported as abnormal.

The final neurological diagnosis was reported as Guillain-Barré syndrome in 46 cases (80.7%) and transverse myelitis in four (7.0%) (Table 5). The remaining seven diagnoses included viral myelitis (1), 3rd cranial nerve palsy (1), hypotonic acute areflexia (1), acute demyelination (bulbar and lumbar) (1), 10th cranial nerve palsy (1), anterior horn disease (non-polio) (1), and demyelinating polyneuropathy (1).

Fifty-six of the 57 cases (98.2%) required hospitalization for periods ranging from one to over 60 days (mean, 10 days); three cases were hospitalised for 30 days or longer. Of the total of 57 cases, nine (15.8%) were fully recovered at 60 days after the onset of paralysis, nine (15.8%) had recovered partially with residual weakness, and one (1.7%) had a stable or progressive

condition. For the remaining 38 cases, recovery status was unknown at 60 days after the onset of paralysis.

Discussion

The 57 AFP cases identified to date for 2000 indicate that the surveillance system continues to be sensitive enough to detect almost all expected cases in Canada, according to the WHO criteria, for the non-polio AFP cases in the targeted population (children under 15 years) in the absence of circulation of wild poliovirus. For the corresponding period for 1999, a total of 59 cases reported initially, but the final number has increased to 61 with the inclusion of two additional cases reported in 2000.

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 less than 15 years in 1996 (30 cases) to 0.97 per 100,000 in 2000 (57 cases). 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 and reported through IMPACT.

None of the clinical specimens tested, i.e., stool, nasopharyngeal or cerebrospinal fluids, were positive for poliovirus infection.

Also significant is the fact that in 2000, as in 1999, the CPSP was able to maintain the 100% return rate of detailed case-specific information forms for all AFP cases. The return rate was 79% in 1996, 96% in 1997 and 97% in 1998. Although duplicate reporting remains relatively high, in many instances duplicate reports provided additional information not included in the "primary" report, thereby proving to be very useful. Thus, 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).

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Anaphylaxis

Editorial Note: *This summary presents a preliminary description of the findings. A full report will be forthcoming, pending a detailed analysis of the study data.*

Highlights

- Injection of epinephrine, the first-aid treatment of choice in anaphylaxis, was often delayed or omitted.
- Foods, especially peanut, were the most commonly-reported trigger factor for anaphylaxis.
- Most children experiencing severe acute allergic reactions also had other allergic disorders, including asthma.

"Anaphylaxis, defined as a severe acute allergic reaction, is surprisingly common in Canadian infants, children and teens.

Dr. Estelle Simons

Summary

During the year 2000, a total of 491 cases of anaphylaxis in Canadian children and youth, ranging in age from infancy to 18 years, were reported to the CPSP. Anaphylaxis occurred more commonly in the child's home than anywhere else, and foods, especially peanut, were by far the most frequently reported trigger factor. Non-food triggers included latex rubber, insect stings, exercise, medications and biologicals. First-aid treatment commonly consisted of oral diphenhydramine (Benadryl®) or another antihistamine. Epinephrine injection was delayed or omitted in many children.

Thanks to the excellent cooperation of all reporting physicians in the Canadian Paediatric Surveillance Program, the picture of anaphylaxis in Canadian children and youth is being defined. This will eventually lead to improved recognition and treatment of the disorder.

Case definition

A confirmed case is an infant or child 18 years or less with a severe allergic reaction to any stimulus having sudden onset and lasting less than 24 hours. One or more body systems may be involved and multiple symptoms such as hives, flushing, angioedema, stridor, wheezing, shortness of breath, vomiting, diarrhea or shock may be evident.

1) Provoking factors: foods, insect stings/bites, latex rubber, medications, exercise, cold, or other stimuli.

2) Symptoms: cutaneous, respiratory, gastrointestinal, cardiovascular and/or central nervous system involvement.

3) Documentation:
   - at the time of the episode: clinical history, physical examination, and serum tryptase levels, if available;
   - weeks or months after the episode: skin tests for hypersensitivity to food, insect stings/bites, latex, medications; tests for other provoking factors.

Duration

January 2000 to June 2001

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Cerebral edema in diabetic ketoacidosis

Highlights

- In the year 2000, 10 confirmed and three possible cases of cerebral edema in diabetic ketoacidosis were reported.
- During the first 18 months of the study, three deaths were reported out of 15 confirmed cases.
- Cerebral edema in DKA does occur in some patients prior to initiation of treatment for DKA.

"The broadening of the case definition has resulted in a more complete ascertainment of cases.

Dr. Elizabeth Cummings

Summary

During 18 months of surveillance, 15 confirmed and eight possible cases of cerebral edema in diabetic ketoacidosis (CE-DKA) were reported to the CPSP. The mortality rate of 20% in confirmed cases is significant. The change in case definition to include patients with a profoundly depressed level of consciousness at initial presentation of DKA has allowed more complete capture of cases and accounts for 33% of all reports. Surveillance will continue until June 2001. Following this, a case-control study

with detailed chart review is planned to establish risk factors for CE-DKA.

Background

Cerebral edema is an uncommon but devastating complication of diabetic ketoacidosis (DKA) in the paediatric age group. When it occurs, the rates of mortality or survival with permanent neurological damage are high.[1] Most studies have failed to clearly establish risk factors for cerebral edema, although it is often attributed to factors related to treatment of DKA. A recent large case-control study suggested that the risk of CE-DKA was associated with factors at presentation as well as treatment factors.[2] In this study, CE-DKA occurred more often in patients with lower pCO_2 and higher blood urea nitrogen (BUN) at presentation, when the serum sodium failed to rise during treatment and when bicarbonate was given. The aim of this study is to identify the frequency of this condition in Canada. Through a case-control study, risk factors for CE-DKA will be identified and 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.

Case definition

A. Inclusion criteria

- Children up to their 16th birthday.
- Sudden or unexpected deterioration in level of consciousness in a child or adolescent with DKA*
- Any death in a child or adolescent 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

Results

Of the 27 reports received in the year 2000 (Table 6), 10 were confirmed cases of cerebral edema in DKA based on data provided in the detailed report forms and three were either possible cases or are awaiting confirmation. Eight were duplicate reports and five did not meet the entry criteria due to the age of the patient or the date of the event. One report of death in a child with diabetes was not associated with DKA. Eight of the 10 (80%) confirmed cases occurred in patients with newly diagnosed diabetes.

TABLE 6

Cases of CE-DKA reported to the CPSP July 1999 to December 2000

Status	2000	1999	Total
Number of reports	27	13	40
Confirmed CE-DKA*	10	5	15
Possible CE-DKA	3	2	5
Did not meet entry criteria†	5	2	7
Duplicates	8	4	12
Death not DKA	1	0	1

* Includes cases of death: 2 (2000), 1 (1999), 3 (Total)

† Excluded due to age (1) or date of event prior to July 1999 (6)

* DKA is defined as a pH <7.35 and/or bicarbonate <18 mmol/L in association with diabetes and ketonuria.

For the 15 confirmed reports to date, the mean age (SD) was 8.2 (4.5) years with a relatively equal sex distribution of eight males and seven females. At DKA presentation, the median pCO_2 was 22 mmHg, bicarbonate 5.5 mmol/L and glucose 54 mmol/L. Ten had an acute deterioration in level of consciousness one to six hours after initiation of treatment and six of these had CT scans. Five had CE suspected at initial presentation of DKA due to a profoundly depressed level of consciousness, with four confirmed by CT scan.

With three deaths associated with cerebral edema in DKA, the mortality rate for confirmed cases was 20%. Nine recovered fully and two are neurologically impaired (one unspecified). One death was reported in a child with diabetes but was not associated with DKA. The cause of this death was unclear.

Discussion

The number of reports of CE-DKA to the CPSP continues to be consistent with the estimated rates prior to the start of the study. The mortality rate in confirmed cases is consistent with results found in a recent multi-centre case-control study.[2] Most of the remaining cases were reported to have a full recovery. This finding needs to be confirmed in the chart review but suggests that prognosis of survivors may not be as poor as was previously reported.[1]

After review of reports from the first six months of surveillance, the inclusion criteria were revised to include patients with a profoundly depressed level of consciousness at initial presentation of DKA. This change proved to be valuable, as 33% of the confirmed cases presented in this way. This rate is much higher than previously reported and has implications for the pathophysiology of CE-DKA, which is controversial but is often attributed to medical treatment. In patients presenting with DKA and profound depression in level of consciousness, the presence of CE should be suspected. Imaging studies may be helpful to confirm the diagnosis.

After two years of surveillance, extensive chart reviews with case controls are planned to determine factors associated with CE-DKA. Sincere thanks to all those who have reported cases. This ongoing collaboration that will continue into a chart review process is greatly appreciated.

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Congenital rubella syndrome

Highlights

- Only one infant born with congenital rubella syndrome was reported to the CPSP in 2000.
- Failure to screen the mother in the first pregnancy led to a missed opportunity of postpartum vaccination and prevention.

"Both rubella and congenital rubella have been virtually eliminated in Canada, thanks to the successful immunization program.

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. Some jurisdictions used MR vaccine for their second dose catch-up campaigns.

Since 1970, the incidence of rubella in Canada has declined markedly; fewer than 50 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 congenital rubella syndrome (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 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.

Case definitions

Confirmed case

Live birth

Two clinically compatible manifestations (any combination from Table 7, 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 7

Congenital rubella syndrome: clinically compatible manifestations

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

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 levels by any standard serological assay;

or

- positive serologic test for rubella-specific IgM;

or

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

Duration

January 1996 to December 2004

Methods

From January 1996 to December 2000, 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/territorial public health authorities were consulted to determine if cases had been previously reported.

Results

In 2000, the CPSP reported a total of three cases, including one newborn (confirmed) and two older children, aged nine years and 15 years, both with late manifestations of CRS (discarded). However, during the same period,

* 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.

two newborn cases with CRS were reported to the NDRS, including the one identified by the CPSP and a second case currently being investigated. This report summarizes the findings of the one case reported to the CPSP.

The infant was born with patent ductus arteriosus, mental retardation, jaundice, purpura, radiolucent bone disease, progressive panencephalitis, bilateral hydronephrosis, hypoglycemia, transient thrombocytopenia, and Wilms' tumor. Rubella virus was cultured from the baby's throat and urine specimens collected 13 days after birth. Persisting rubella-specific IgG was present but was negative for rubella-specific IgM.

The Canadian-born mother previously delivered a healthy child in a hospital (rural) setting. Rubella vaccination status of the mother is unknown and she doesn't ever recall having received any rubella vaccine, including at the time of the first postpartum hospital discharge, or having had any rubella screening. She does not recall having any contact with a rubella case or having any symptoms compatible with rubella during pregnancy.

Discussion

The 2000 case history indicates that the mother did not have any rubella vaccination and was susceptible to rubella even during her first pregnancy; fortunately, she was not exposed to rubella at that time. It appears that no screening for rubella susceptibility was done during the health care visits or any rubella immunization offered at any time before the second pregnancy, including just before the postpartum hospital discharge. Since rubella transmission in the general population has been on the decline, secondary to successful rubella vaccination, only very limited naturally acquired immunity due to wild virus infection is present. Rubella vaccination before pregnancy is the only measure to protect the fetus from potential maternal infection.

The very low incidence of CRS, CRI and rubella infection suggests that Canada is getting closer to achieving the goal of eliminating indigenous rubella infection during pregnancy.

From January 1996 to December 2000, with national surveillance in place, seven new cases of newborns with CRS were reported in Canada (Table 8). Two were born to immigrant woman, one to an aboriginal woman, and two to non-aboriginal women. These five 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. Prenatal rubella screening and postpartum vaccination will continue to be essential in our quest to eliminate rubella infection during pregnancy.

TABLE 8

Cases of CRS by year of birth reported to CPSP/IMPACT and NDRS, January 1996 to December 2000

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
2000	1	0	1	2
Total	**2**	**0**	**5**	**7**

* NDRS data is provisional

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Hemolytic uremic syndrome

Highlights

- HUS associated with diarrhea (HUS D+) is still a serious disease as two deaths were confirmed in the first eight months of the study, and 17 of the 61 cases needed dialysis.
- *Escherichia coli* O157 remains the most frequent culprit of HUS D+.
- No cases of *Streptococcus pneumoniae* HUS were reported.

Dr. François Proulx

"HUS remains a leading cause of acute renal failure in children.

Background

Hemolytic uremic syndrome (HUS) is one of the leading causes of acute renal failure in many developed countries, including Canada.[1] Most commonly HUS is associated with prodromal symptoms, including diarrhea, bloody stools and vomiting. Cases may occur singly or in outbreaks, in families or linked to specific events related to ingestion of contaminated food or water. For example, a waterborne outbreak in Ontario in the summer of 2000 resulted in over 2000 cases of *E. coli* and *Campylobacter* infection. Verotoxin-producing *E. coli* (VTEC) infection in a number of cases was associated with development of HUS.[2] VTEC is frequently associated with HUS. However, HUS may also occur with neuraminidase-producing pathogens such as

S. pneumoniae. *S. pneumoniae* associated HUS (SPAH) has a significantly higher mortality rate in children than HUS with diarrhea.[3]

Paediatricians participating in the surveillance program report cases of HUS with prodromal diarrhea (HUS D+) and without diarrhea (HUS D–). All detailed case reports were reviewed and cases fulfilling the D+ and D– case definitions were included in the study.

Objectives

1. To determine the incidence of HUS D+, including illness caused by *E. coli* O157:H7 and other VTEC serotypes.
2. To determine the incidence of invasive SPAH.

Case definitions

HUS D+ Diarrhea associated with HUS: A prodrome of enteric symptoms in a child under 16 years of age with: acute renal impairment with increased serum creatinine;* microangiopathic hemolytic anemia;† thrombocytopenia‡ in the absence of septicemia, malignant hypertension, chronic uremia, collagen or vascular disorders. These criteria may not all be present simultaneously and may be accompanied by neurological impairment.

HUS D– *S. pneumoniae* associated HUS (SPAH): A child under 16 years of age with evidence of invasive *S. pneumoniae* infection: (blood or another normally sterile biological fluid: cerebrospinal, pericardial, articular, peritoneal, pleural) excluding middle ear, sinus, tracheal aspirates; and renal impairment and hematological organ failure defined as acute renal impairment with increased serum creatinine;* microangiopathic hemolytic anemia;† thrombocytopenia‡ in the absence of septicemia, malignant hypertension, chronic uremia, collagen or vascular disorders. These criteria may not be present simultaneously and other organ failures may occur.

A definite case of SPAH requires evidence of thrombotic microangiopathy on renal biopsy or autopsy. Distinction between pneumococcal sepsis with secondary organ failures (RHOF-ISP)§ and SPAH will be determined through a Delphi process.

Duration

April 2000 to March 2002

Methods

Paediatricians participating in the CPSP are requested to report all cases of HUS, with or without prodromal enteric symptoms. All case reports are reviewed to determine whether they fulfill the case definitions for HUS D+ or D–. Detailed review is particularly important where all components of the case definitions are not met simultaneously or where the results of diagnostic tests lie just outside the definition threshold. Duplicates are removed and all cases under review retain pending status until HUS is confirmed.

Results

During the first eight months of the study for which reports have been received, a total of 122 initial reports of HUS were received. This total included 76 (62%) that were confirmed as HUS D+, 34 that were duplicates and six that did not meet the HUS case definition. The status of the remaining six is currently

TABLE 9

Age distribution of confirmed HUS D+ cases from April to December 2000

Age group (years)	Number of cases (%)
0-1	3 (5)
1-4	34 (56)
5-9	19 (31)
10-15	5 (8)
Total	**61 (100)**

* serum creatinine: >50 μmol/L if <5 years; >60 μmol/L if 5-9 years; >90 μmol/L if 10-13 years; >110 μmol/L if >13 years

† Hb: <100 g/L with fragmented red cells

‡ platelets: <150,000 x 10^9/L

§ Renal-hematological organ failures associated to invasive *S. pneumoniae*

pending. Of the 76 confirmed cases, 35 were males and 41 were females. No reports of *S. pneumoniae* HUS were received during this period.

Detailed reports were received for 61 cases ranging in age from seven months to 15 years (Table 9). Over half the cases were aged one to four years and almost a third were in the five to nine years age group (median age was three years seven months).

Fifty-nine cases presented with symptoms of diarrhea, including 52 with bloody diarrhea. Two confirmed cases did not record diarrhea as a presenting symptom: for one of these cases, information on diarrhea was not stated; for the other case that was negative, the patient presented with vomiting only. A total of 17 children required dialysis; 10 cases were evaluated for long-term renal impairment and three children were being treated for other sequelae of HUS. Two of the 61 confirmed cases died, 42 cases had a pathogen identified. Of the 40 *E. coli* isolates identified, 39 were identified as *E. coli* O157, of which 16 were identified as *E. coli* O157:H7.

Summary

The number of confirmed cases reported during the first eight months of the study is slightly higher than expected. This may be explained by a large cluster associated with a waterborne outbreak in Ontario in the summer of 2000. The high proportion of cases aged one to four years and the median age (three years seven months) is consistent with previous reports.[4] Finally, during this eight-month study period, all cases were classified as HUS D+ and *E. coli* O157 was the predominant pathogen identified.

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Hemorrhagic disease of the newborn

Highlights

- One baby with hemorrhagic disease of the newborn who did not receive vitamin K prophylaxis was reported in 2000.
- With only five confirmed cases in four years, this study reinforces the effectiveness of the CPS guidelines of routine administration of vitamin K to newborns.

"Hemorrhagic disease of the newborn may occur when no vitamin K is given and is potentially lethal or permanently disabling.

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 in 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 that 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.

Duration

January 1997 to December 2000

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 four reports received in 2000, one baby with HDNB was an unplanned home birth at 36 weeks gestation who was then admitted to hospital for a two-week stay. The baby was breastfed and presented at 31 days of life with intracranial bleeding (left parietal hemorrhagic infarct, intraventricular hemorrhage). Coagulation profile was compatible with HDNB. The baby who had not received vitamin K following birth has been left with "extensive brain damage".

Of the remaining reports, one was a duplicate of the first case and another was a late report for 1998. A third baby was felt not to have HDNB after presenting with gastric bleeding (later evidence of gastric hemangiomas) and disseminated intravascular coagulopathy.

A poster report of HDNB to the Canadian Paediatric Surveillance Program 1997 to 1999 was presented at the 2000 annual meeting of the Canadian Paediatric Society.[2] Conclusions were:

- In spite of detailed instructions, HDNB is often confused with hemolytic disease of the newborn. (This is probably why the follow-up British study is called vitamin K deficiency bleeding.)
- Diagnosis of HDNB is often made without coagulation studies or with studies not compatible with vitamin K deficiency.
- The incidence of HDNB in Canada appears to be one in 140,000 to one in 170,000 births.
- In Canada, HDNB most often presents with intracranial bleeding that may have serious sequelae.
- Not all babies in Canada receive vitamin K following birth; the relative incidence of HDNB in babies given intramuscular versus oral vitamin K is not distinguishable.

TABLE 10

Vitamin K administration in HDNB cases 1997 – 2000

Vitamin K	Intra-muscular (IM)	Oral (PO)	Not received
Number of cases	2	1*	2

* Patients also had biliary atresia.

Conclusions

- One report of HDNB was confirmed in a baby who was born at home at 36 weeks gestation and subsequently cared for in hospital with no vitamin K prophylaxis.
- HDND is rare in Canada supporting the effectiveness of the Canadian Paediatric Society guidelines.[1]

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Neonatal herpes simplex virus infection

Highlight

- In the first three months of the study, one infant with HSV-2 infection that disseminated to the central nervous system (CNS) was diagnosed at birth and died at three days of age.

"The majority of untreated cases of disseminated neonatal herpes infection will die and most survivors will suffer from severe neurological sequelae. It is essential to identify the true incidence of neonatal herpes simplex virus infection in Canada and its impact on surviving infants to further strengthen recommendations on prevention and control strategies.

— Louise Cormier

Background

Genital herpes simplex virus (HSV) and neonatal HSV infections are reportable diseases in some Canadian provinces and territories; however, the epidemiological information collected through this passive surveillance system is limited. This infection is not included in the notifiable diseases system at the Federal level. It is therefore not possible to determine accurately the prevalence, incidence and trends of neonatal herpes infection in Canada. Data collection is essential to better understand the epidemiology and to monitor the trends. Canadian data on morbidity, mortality and the mother and infant risk determinants will allow comparison of neonatal herpes infection rates with other countries. It will also provide baseline data before a vaccine becomes available. The information will be used to promote prevention, control program strategies and further research and to estimate the burden of illness in Canada.

HSV infections pose a serious public health concern, especially since high proportions of these infections are unrecognized. The most serious direct consequence of genital HSV infection is the perinatal transmission from mother to infant. Almost all cases of neonatal herpes are perinatally acquired at the time of delivery.[1] The disease in neonates is also more difficult to diagnose since clinical signs are non-specific and must be confirmed by laboratory testing.[2,3]

If genital HSV infection in Canadian women follows the same increasing trend as in the United States (US), the incidence of neonatal herpes might rise. The expected number of cases may vary between eight and 183 using the incidence rates of the United Kingdom or Australia (2/100,000 live births) and the US (50/100,000 live births).[4] In 1999, the neonatal HSV infection estimate for the province of Ontario was 6.8 cases per 100,000 live births (eight cases reported). Therefore, the overall Canadian incidence rate for neonatal herpes infections could be higher than the British and Australian rates.

The provision of an uninterrupted flow of information (between the principal investigator and the health providers) is essential.

Method

This surveillance project consists of two phases. Phase I will collect non-nominal data through the CPSP until the fall of 2003. A detailed reporting questionnaire will be used to collect data on HSV infection, including neurological and other complications, and mother and infant risk determinants. In Phase II, working in collaboration with reporting physicians and paediatricians, the Division of Sexual Health Promotion and STD Prevention and Control (Health Canada) will follow up, annually, for a period of three years, the cohorts of HSV-infected infants identified in Phase I to determine outcomes.

Cases reported through the active surveillance study will be validated through the Canadian Institute of Health Information (CIHI) and through yearly projected laboratory surveys of HSV tests.

An evaluation of the data collection process will be done upon completion of the first year for both phases.

Objectives

1. To estimate the incidence rate of neonatal herpes infection (HSV-1 and HSV-2) for the years 2000 to 2003 per 100,000 live births in Canada.
2. To determine the proportion of HSV-infected infants with localized diseases, encephalitis or disseminated diseases.
3. To identify risk determinants in mothers and to assess their maternal HSV status prior to delivery.
4. To analyze trends of reported cases over a minimum period of three years by age, sex and province.
5. To document the morbidity/mortality of neonatal infections for the years 2001 to 2006, through a cohort study of infants identified in each of the first three years of the project.

Case definition

For the purpose of this study, the neonatal period is being extended to 60 days of life so that late diagnoses are not missed. This will optimize the capacity to identify the maximum number of cases.

All cases will be laboratory-confirmed and comprise at least one of the following:

1. **Culture:** Isolation of herpes simplex virus (HSV-1, HSV-2) from any site in an infant equal to or less than two months (60 days) who demonstrates one of the following:
   - Localized infection involving the skin, eyes or mouth
   - Disseminated infection:
     a) to the central nervous system (encephalitis);
     b) to organs other than CNS

2. **Serology:** Herpes simplex virus IgM in infants equal to or less than two months (60 days) of age in conjunction with one or more of the following clinical signs: herpetic vesicular lesions to skin, mouth or eyes, keratoconjunctivitis, retinal dysplasia, chorioretinitis, cataract, encephalitis, lethargy, seizures, tremor, poor feeding, bulging fontanel, irritability, respiratory distress, jaundice, bleeding diatheses, shock, pneumonitis, disseminated intravascular coagulopathy.

   A repeat serology (HSV IgM) after three or four weeks of onset of illness if test was negative initially will be acceptable.

3. **PCR:** On cerebrospinal fluid (CSF) and other tissues.

Duration

Phase I through the CPSP – October 2000 to September 2003

Phase II through Health Canada – Follow-up of three successive cohorts of HSV infected infants for a period of three years each – October 2001 to September 2006.

Results

In the three-month period from the start of the study on October 1, 2000, nine initial forms reporting possible cases of neonatal herpes infection were sent to the CPSP. Of the nine reported cases,

one was a duplicate, two did not meet the case definition (one was diagnosed prior to the study period and the other was not laboratory-confirmed), two were laboratory-confirmed, and four are still under investigation.

The first case of neonatal HSV type 2 encephalitis was confirmed in a neonate with a positive HSV-PCR on cerebrospinal fluid and an MRI showing severe cystic encephalomalacia. The 25-year-old mother acquired primary genital HSV-2 infection during the first trimester of her pregnancy. Although she had no genital lesion at the time of delivery, a cesarian section was performed due to fetal distress at week 27 of the pregnancy. The newborn weighed 1010 grams and had an Apgar of eight at five minutes. Even with initiation of intravenous acyclovir at birth, following laboratory testing, the infant died at three days of age.

The second confirmed case was a newborn with localized herpes HSV-1 infection to the skin and mouth. A culture of the lesions confirmed the case 13 days after birth. The 16-year-old mother had a vaginal delivery, free of complications at 41 weeks' gestation. She was asymptomatic at delivery and had no known history of HSV infection; she could not recall any symptoms suggestive of oral or genital HSV infection. At birth, the baby weighed 3770 grams and had an Apgar of 10 at five minutes. The infant was treated with intravenous acyclovir and survived. At the time of diagnosis, no obvious sequelae were present and it was too early to evaluate the child's developmental impairment.

Neither of the above two cases were diagnosed with congenital toxoplasmosis, congenital rubella, or cytomegalovirus infection.

Discussion

At this point, the number of neonatal HSV infection-confirmed cases is too small to draw any conclusion. The first case showed the severity and the devastating effect of neonatal HSV infection but was the infant's death due to an HSV infection or prematurity? Is neonatal HSV incidence and mortality higher among infants born to young mothers? Primary genital HSV infection is anticipated to affect younger mothers. The active surveillance study of neonatal herpes infection will provide some answers to infection trends in the Canadian population.

To evaluate the consequences of neonatal HSV infection on surviving children, it is essential, as planned in Phase II of the study, to follow the surviving children annually for at least three consecutive years.

Summary

From October 1 to December 31, 2000, two confirmed cases meeting the case definition criteria were reported. Four possible cases are still under investigation.

Of the two confirmed cases, one infant died three days after birth and was diagnosed with HSV-2 infection disseminated to the central nervous system. The other infant was diagnosed with HSV-1 infection localized to skin and mouth and survived. The total number of laboratory-confirmed neonatal herpes cases for this period might increase due to reporting delay. The follow-up time is too short to assess specific outcomes of this infection on the surviving case.

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Funding

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Progressive intellectual and neurological deterioration

Highlights

- No cases of variant Creutzfeldt-Jakob disease have been reported since surveillance commenced in July 1999.
- In the eighteen-month period since the start of the study, 50 of the 83 reports received have been classified as having a progressive neurological syndrome associated with intellectual deterioration.
- A definite diagnosis was available in 42 cases, representing 19 known degenerative diseases. The most common diagnoses were mitochondrial disorders (eight), ceroid lipofuscinosis (eight) and Krabbe's disease (four).

"Variant Creutzfeldt-Jakob disease has not been detected in Canada, but progressive childhood neurological disorders do occur and are caused by many different degenerative diseases.

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. All reported cases were reviewed by the principal investigator and classified into one of four predetermined categories. Cases with evidence of neurological and intellectual regression without known cause were reviewed by a panel of paediatric neurologists. 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 (CJD-SS) team for further investigation. Cases referred to the CJD-SS were to be monitored through their lives and investigated at death, unless elements of the case warranted 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 case investigation by enrolling the case in the Canadian CJD surveillance system.

Case definition

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 patients meeting the above criteria for the diagnosis 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 a diagnosis made by a paediatric neurologist, only the diagnosis 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. This data was reviewed by the principal investigator and patients were classified into one of four groups. **Group A** consisted of patients with clinical evidence of progressive intellectual and neurological deterioration and sufficient information to make a diagnosis. **Group B** included patients with a history compatible with the diagnosis of either the classic or variant forms of Creutzfeldt-Jakob disease. This group of patients was referred to the CJD surveillance program 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 three paediatric neurologists, one medical geneticist and a paediatric neuropathologist 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**, consisted of patients awaiting further information from the referring clinician before classification.

Results

From the onset of this project, 83 possible cases of progressive neurological and intellectual deterioration have been reported to the CPSP (41 cases from July to December 1999 and 42 cases in 2000). Eleven cases were duplicates. Forty-nine cases were classified as having a progressive neurological syndrome associated with intellectual deterioration (Table 11). A definite diagnosis was available in 42 of the reported cases. In the remaining eight cases the clinical history is strongly suggestive of a neurodegenerative disorder but at the time of this report a definite diagnosis has not been made. Only one case of iatrogenic Creutzfeldt-Jakob disorder has been reported to date. This case in 1999 was also reported independently to the CJD-Surveillance System Canada. Fourteen cases were felt not to meet the above-mentioned entry criteria. This group of patients represented either static encephalopathies, such as chromosomal disorder,

TABLE 11

Summary of progressive intellectual and neurological deterioration in children

	Total	1999	2000
Creutzfeldt-Jakob disease	1	1	0
Mitochondrial disorders	8	6	2
Krabbe's disease	4	4	0
Cree encephalopathy	2	2	0
Rett's syndrome	3	1	2
Adrenoleukodystrophy	2	1	1
Hurler's syndrome	3	2	1
Gaucher's disease	1	1	0
Fumerase deficiency	1	1	0
Mucopolysaccharidosis type pending	1	1	0
Ceroid lipofuscinosis	8	2	6
Sanfilippo's syndrome	1	0	1
Pyruvate dehydrogenase deficiency	1	0	1
Hunter's syndrome	1	0	1
Biotinidase deficiency	1	0	1
Alexander's disease	1	0	1
Glucose transport defect	1	0	1
Neiman Pick type C	1	1	0
Undiagnosed neurodegenerative disorders	8	2	6
Duplicates	11	5	6
Not meeting criteria for PIND disorders	14	8	6
Insufficient data	9	3	6

or non-progressive acute encephalopathies post-infective or traumatic in nature. One case of acute neurological dysfunction secondary to rabies was reported. Nine cases are still waiting information necessary for classification. Three of these cases date back to the onset of this study in July 1999. Difficulty in getting this information has resulted from the limited information submitted by physicians on the original mail-back forms. Letters asking for this information often have gone unanswered. Direct telephone conversations with the physicians have in a few cases proven helpful in getting the missing information. Often, when contacted, the physicians have forgotten who the patient was or have referred the patient to a university centre for confirmation of diagnosis. Without consent for release of information, the physicians in the referral centres who have been asked to see the child in consultation have been reluctant to release the necessary information to the surveillance program.

The rate of reporting of possible cases has remained fairly stable over the period of the study. The return rate from across the country has continued to be representative of the provincial population densities.

Summary

Cases meeting the criteria for entry into this study have accrued at the expected rate. No new cases of variant Creutzfeldt-Jakob disorder have been discovered in 2000. The only known case of CJD reported to this surveillance program was also reported independently to the CJD-Surveillance System Canada. Cases of progressive intellectual and neurological disorders in children are rare events.

Acknowledgements

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Smith-Lemli-Opitz syndrome

Highlights

- All the patients with confirmed SLO, from whom appropriate samples were received, had both *DHCR7* mutations identified.
- Identification of *DHCR7* mutations allows for genetic counselling, carrier testing, and prenatal diagnosis in family members at risk.

"Smith-Lemli-Opitz syndrome has recently been found to be much more common and variable than previously thought with cases diagnosed ranging from fetuses with lethal malformations to children with intellectual deficits and autistic behaviours.

Dr. Małgorzata Nowaczyk

Background and rationale

Smith-Lemli-Opitz syndrome (SLO) is an inherited defect of cholesterol synthesis caused by mutations in the 7-dehydrocholesterol reductase gene (*DHCR7*). 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 characteristic syndrome of multiple malformations, dysmorphic features, mental retardation, and behavioural abnormalities. SLO is readily diagnosed by demonstration of elevated levels of the cholesterol precursor 7-DHC that accumulates in body fluids and tissues of these patients. The use of a biochemical diagnostic test for SLO has led to the diagnosis of SLO in fetuses and in infants with multiple or lethal anomalies that previously defied diagnosis, as well as in individuals who have significant mental retardation and behavioural abnormalities, but minimal physical features. Many of the latter group of patients escaped detection for long periods of time; some were diagnosed with idiopathic mental retardation, pervasive developmental disorder, or autism. The behavioural phenotype of SLO is characterized by autistic features, tactile defensiveness and significant sleep disturbance among other features. Treatment of SLO with dietary cholesterol supplementation has shown promise with improvement in the general health, as shown by reduction of frequency of infections, improved growth, and significant improvement in behaviour. Families of children with SLO treated with cholesterol supplementation report great improvement in the quality of life in addition to the physical improvements. It is possible that early institution of treatment may improve the final developmental outcome of patients with SLO; thus, if SLO has a sufficiently high incidence, newborn screening of SLO may be indicated.

Objectives

1. To determine the incidence and prevalence of inherited deficiency of 7-dehydrocholesterol reductase in Canada by ascertaining all newly diagnosed cases of SLO, and by confirming the clinical diagnosis in probable cases by demonstrating elevated 7-dehydrocholesterol level in plasma, or in blood obtained in neonatal screening blood spots.
2. To determine if prenatal and neonatal screening for SLO is indicated in Canada.
3. To obtain demographic and medical information on patients with SLO and to assemble a database for demographic studies and for future research use (e.g., evaluation of dietary and medical therapies, genotype-phenotype correlation).

Case definition

Confirmed case:
Elevated concentration of 7-dehydrocholesterol (7-DHC) in plasma (postnatal), or in chorionic villus sample or amniotic fluid (prenatal), or in blood spots obtained as part of neonatal screening.

Probable case (requires biochemical or DNA confirmation):

A. Infant/child/adult with developmental delay/mental retardation, with behavioural abnormalities/attention deficit hyperactivity disorder (ADHD)/autistic features, with normal chromosomes, and any two of the following features:
   i. 2-3 toe syndactyly (webbing)
   ii. index finger clinodactyly ("zig-zag" index finger)
   iii. abnormal facial features (epicanthal folds, short nose, micrognathia)
   iv. ptosis
   v. genital anomalies in the male
   vi. failure to thrive or low birth weight
   vii. feeding difficulties requiring gavage or tube feeding

B. Stillbirth or newborn with normal chromosomes and any two of the following features:
   i. sex reversal/ambiguous genitalia/genital anomalies in male infant
   ii. abnormal facial features (epicanthal folds, short nose, micrognathia)
   iii. cleft palate/submucous cleft
   iv. polydactyly of hands or feet
   v. lobster-hand deformity or missing fingers of hand
   vi. 2-3 toe syndactyly (webbing)
   vii. internal anomalies (any of the following: cystic renal dysplasia, renal agenesis, nervous system malformations, unilobar lungs, adrenal lipid accumulation, cardiovascular malformations, punctate stippling of epiphyses)
   viii. low unconjugated estriol on maternal serum screening during the second trimester of pregnancy

C. Previous clinical diagnosis of SLO without documented elevation of 7-DHC or known *DHCR7* mutations.

Duration

January 2000 to December 2002

Results

TABLE 12

Results for year 1: January – December 2000

Reported	Confirmed	Duplicates	Discarded	Pending
36	19	9	6	2

Discussion

Nine confirmed new cases, born or predicted-to-be born between November 14, 1999 and October 18, 2000 were reported, yielding an expected incidence of one in 37,100 births across Canada. All, but one, were cases of severe SLO, and two were pregnancies that were stopped because of multiple malformations. All of the cases of SLO were reported in infants of European Caucasian origins, suggesting that the incidence of SLO in Canadians of European Caucasian origin is one in 29,700.

The report of only one patient with mild SLO born last year further confirms the need for extended surveillance to capture the mild cases of SLO. Information about older patients previously diagnosed with SLO was received and included in the growing SLO patient database, expanding our understanding of the prevalence of this condition and the proportion of milder cases who survive

into teenage years and adulthood. In addition, the paucity of prenatally lost cases of SLO that were reported to the CPSP further suggests that the most severely affected cases may escape diagnosis.

All of the patients reported to the CPSP and confirmed to have SLO underwent mutation analysis to detect mutations causing SLO. In all cases both mutations were identified. The identification of *DHCR7* mutations allows for early prenatal diagnosis in future pregnancies for couples at risk, and for carrier identification for members of extended families. An extensive database of SLO-causing mutations in the Canadian patients, including mutations and their origins in the French-Canadian population and in Southern Slavs, Tatars (Central Asians), and Russians has been assembled. Two new *DHCR7* mutations have also been identified. This new information is being added to known-international databases to increase the understanding of genotype-phenotype correlation.

Thanks to the participation and cooperation of all the physicians who contribute to the success of the CPSP, the study is on its way to meeting the objectives set up at the beginning of the study. Thank you!

The following publications resulted from the information obtained through the CPSP surveillance program for SLO.

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Funding

Hamilton Health Foundation

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Subacute sclerosing panencephalitis

Highlights

- Since the beginning of the surveillance in 1997, only three cases of SSPE have been reported (one delayed report from 1995 and two confirmed in 1999).
- All three have a high suspicion of being related to wild measles virus infection, thus confirming the efficacy of the present measles program.
- Although SSPE will no longer be part of the active surveillance program, case reports on SSPE should be sent to the provincial health departments and the Division of Immunization at Health Canada.

> *All SSPE cases should have brain biopsy material analysis to identify the measles virus.*
>
> — Dr. Wikke Walop

Background

Globally, between 30 and 40 million cases of measles occur annually. It still ranks as a major cause of childhood mortality with about one to two million deaths annually. Approximately 0.1 percent of cases of measles infection result in an acute post-infectious measles encephalitis, with a mortality rate of 10 to 30 percent.[1] The mechanism of action is thought to be an autoimmune reaction against brain antigens caused by the measles virus.

Two serious late complications due to measles infection are subacute sclerosing panencephalitis (SSPE) and, in immunocompromised individuals, measles inclusion body encephalitis (MIBE). Both diseases are fatal.[2] SSPE is a neurodegenerative disease caused by a persistent infection with an altered form of the measles virus and has been the focus of active surveillance.[3]

Objectives

SSPE surveillance has been in place for the years 1997-2000. Active surveillance for this disease was put into place to reassure the public, and Health Canada, about the relative safety of measles immunization, compared with wild virus infection.

Case definitions

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).

Duration

January 1997 to December 2000

Results

One case was reported in 1997 but had been initially diagnosed in 1995. The 20-year-old male had not been immunized and had measles at the age of three years. He presented with a history of forgetfulness and hand tremors, with slowness in walking and hunching after an episode of chickenpox. Learning difficulties were also present. Positive investigations included elevated serum and CSF measles antibodies, and an EEG with stereotyped periodic sharp and

slow-wave discharges every five to seven seconds. This overall pattern and clinical interpretation was suggestive of SSPE.

The other two cases were diagnosed in 1999 and were associated with a high index of suspicion of a prior episode of measles.

The presenting symptoms for a 16-year-old male included a diffuse general rash followed by decreased memory, decreased social interaction and language difficulties, and a recent onset of myoclonic jerks. Laboratory tests of the cerebrospinal fluid and serum were positive for IgG. Diagnostic imaging found that the focal signal abnormalities are those as described in a patient with a clinical suspicion of SSPE.

The second case had been vaccinated at age one. At age six, obscure seizures started, followed by generalized clonic seizures, two episodes of status epilepticus, and then atonic seizures. Two years later he developed right-sided neglect, then ataxia, followed by loss of intellect ability. Although there is no known history of measles infection, there is a history of a rash. An EEG showed periodic complexes, with generalized slowing. The measles IgG titre was 80, the IgM not determined. The CSF IgG titre was 240.

No cases were reported for the year 2000.

Discussion

One of the most important aspects of the CPSP as an active surveillance program is its systematic approach to case finding. Although this active phase of surveillance has ended, it remains important with the elimination of indigenous measles in Canada and high coverage with measles vaccine that all cases of SSPE be fully identified. Any such cases of SSPE should continue to be reported to the Division of Immunization at Health Canada.

It remains important to follow up all suspect cases with laboratory investigations to determine the serum and CSF levels of IgG antibody. Actual titre values are preferred over more general terms, such as positive or negative. Brain biopsy material should be sent to the Viral Exanthemata Laboratory* to determine vaccine versus wild-type strain differentiation for measles, rubella and varicella-zoster viruses.

Conclusion

The Division of Immunization at Health Canada hereby acknowledges the support given by the CPSP and its participants, the paediatricians across Canada, and the staff at the Canadian Paediatric Society. Without their diligence rare cases would go undetected. Thank you.

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2. Gascon GG. Subacute sclerosing panencephalitis. Sem Pediatr Neurol 1996; 3: 260-9.
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Funding

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2000 Results

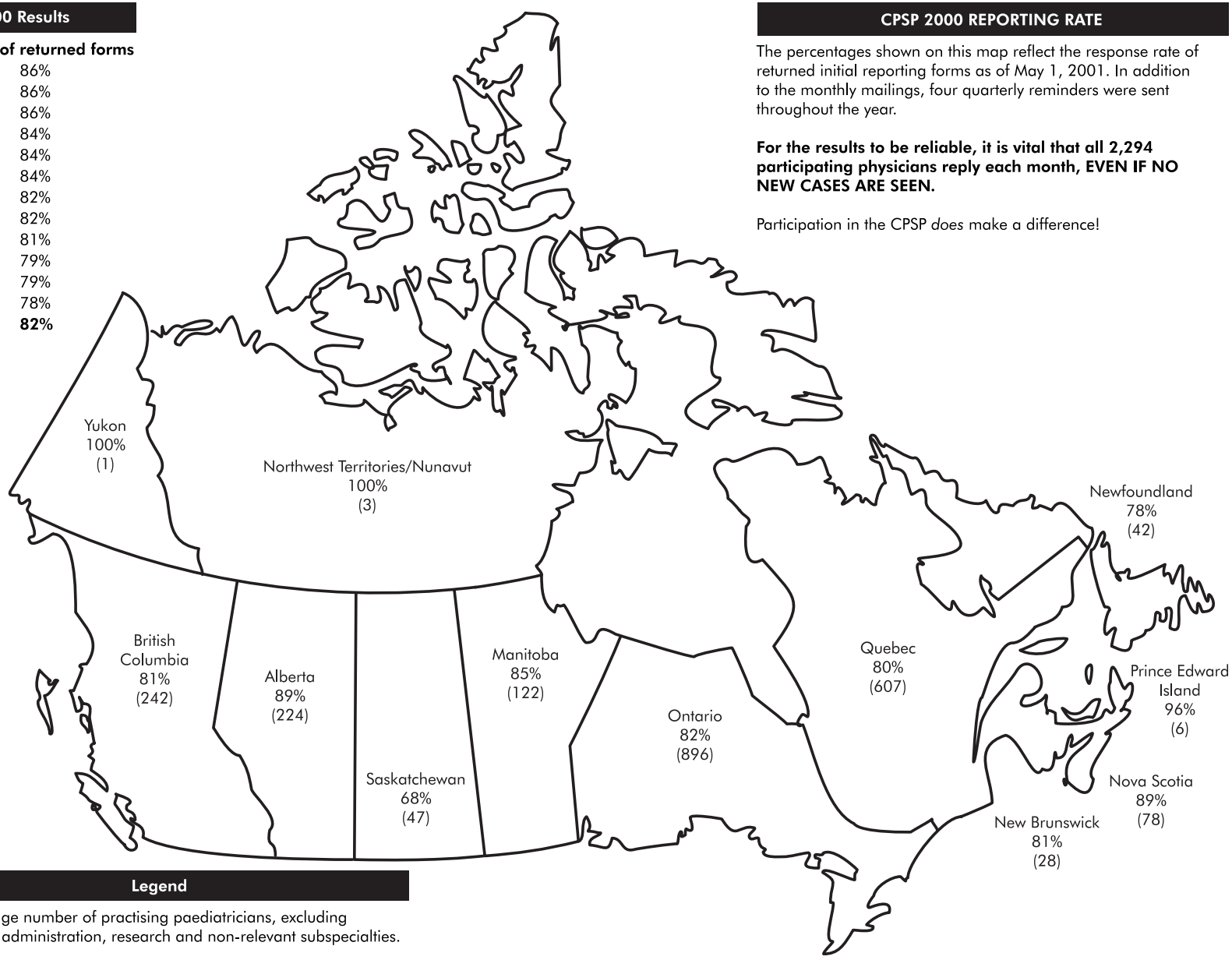
Percentage of returned forms	
January	86%
February	86%
March	86%
April	84%
May	84%
June	84%
July	82%
August	82%
September	81%
October	79%
November	79%
December	78%
Average	**82%**

CPSP 2000 REPORTING RATE

The percentages shown on this map reflect the response rate of returned initial reporting forms as of May 1, 2001. 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 2,294 participating physicians reply each month, EVEN IF NO NEW CASES ARE SEEN.

Participation in the CPSP *does* make a difference!



Legend

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

New Studies in 2001

Hepatitis C virus infection

Dr. Normand Lapointe

"The economic burden associated with hepatitis C virus disease underscores the importance of prevention, early identification and treatment of HCV infection.

Hepatitis C is now recognized as the most common cause of chronic viral hepatitis leading to cirrhosis, end-stage liver disease and hepatic carcinoma. Hepatitis C infection could be underestimated in children.

The CPSP offers a unique opportunity to delineate the epidemiology of hepatitis C virus (HCV) infection among children and adolescents, to establish the regional distribution and to estimate modes of transmission. Furthermore, this study intends to define, prospectively, the natural history of HCV infection and to describe the current management of HCV-infected children. Information compiled in the surveillance program will be used to facilitate new clinical and basic studies. The study will provide an excellent opportunity to analyze combined Canadian, British and Irish data. Improved understanding of the Canadian situation should impact future public health actions.

Duration

February 2001 to January 2003

Funding

Hepatitis C Division, Centre for Infectious Disease Prevention and Control, Population and Public Health Branch, Health Canada

Principal investigator

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Neonatal liver failure/perinatal hemochromatosis

Dr. Eve Roberts

"Neonatal liver failure presents unique clinical challenges and may not be as rare as currently thought. Early diagnosis, supportive medical care, and specific treatments or liver transplantation can be lifesaving.

Neonatal liver failure (NLF)—severe liver dysfunction in the neonate—is thought to be rare. It is nearly always

difficult to diagnose and manage. In the past, all NLF has been labeled as "acute" because it has lasted less than eight weeks, but often the infant is also less than eight weeks old! Some infants with NLF have end-stage liver disease with cirrhosis, as a result of liver damage beginning during gestation.

For this study, NLF has been defined as severe hepatic dysfunction with coagulopathy, metabolic instability and signs of liver damage presenting in the neonatal period (occurring in the first 60 days of life). Many infants present with these symptoms soon after birth.

NLF is classified as "acute-pattern" and "chronic-pattern". With the acute pattern, a previously normal liver is damaged by an acute insult, such as herpes simplex infection, resulting in marked rises in serum aminotransferases, jaundice and coagulopathy. In the chronic pattern, significant liver damage is already established, often because of metabolic disease; cirrhosis may be present at birth, with near-normal aminotransferases, coagulopathy, hypoalbuminemia and ascites (possibly fetal ascites).

Perinatal hemochromatosis (also known as neonatal hemochromatosis or neonatal iron storage disease) is a typical example of chronic-pattern NLF. It usually presents early in the newborn period. Characteristic findings include cirrhosis with extensive hepatic and extrahepatic iron-overload but sparing of the reticuloendothelial system. A combination of anti-oxidants with desferroxamine may be lifesaving or at least stabilize the infant until liver transplantation is possible.

The CPSP provides a comprehensive surveillance method to collect information on all cases of NLF in Canada prospectively, with as little ascertainment bias as possible. It is anticipated that the study will find acute-pattern NLF due to viral infections, acute- and chronic-pattern NLF due to hereditary tyrosinemia type 1, and chronic-pattern NLF due to various disorders, notably perinatal hemochromatosis.

As NLF may be more common than is currently appreciated, these data will give unique epidemiological information that should translate into improved methods for diagnosis and treatment.

Duration

February 2001 to January 2004

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Funding

Coady Family Fund for Liver Research

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CHARGE association/ syndrome

"These distinctive looking children with severe medical problems are surviving but often remain undiagnosed. The CHARGE association/syndrome diagnosis is based on defined clinical criteria, which should provide clear indication for diagnosis.

Dr. Kim Blake and three-year-old Kennedy Weir

CHARGE association/syndrome (CAS) is a non-random occurrence of anomalies that occurs together more frequently than one would expect

on the basis of chance. The original diagnostic criteria required the presence of four out of six of the characteristics; **C**oloboma, **H**eart Defect, Choanal **A**tresia, **R**etarded Growth and Development, **G**enital Hypoplasia, **E**ar Anomalies/Deafness. Recently, a medical advisory group working with the CHARGE Association Support Group recognized that some of the original anomalies were less important and that other defects were rising in diagnostic value. The proposed revised diagnostic criteria[1] are major characteristics: Coloboma, Choanal Atresia, Characteristic Ear Anomalies, Cranial Nerve Dysfunction (facial palsy, swallowing difficulties). Minor criteria: Heart Defect, Orofacial Cleft, Genital Hypoplasia, Growth Deficiency Developmental Delay, Tracheoesophageal Fistula and Distinct Face. The diagnosis is firmly established when all four major or three major and three minor criteria are present.

The true incidence of CAS is not known, with estimates ranging from 0.1–1.2/100,000 live births. The Maritime data suggests a much higher incidence of 1/9,000 based on six verified cases diagnosed in the neonatal period in the last three years. The purpose of this study is to determine the true incidence of CAS in Canada. CAS lends itself to collaborative multi-centered research. Particular areas of interest will be the behavioural phenotype, early cochlear transplantation, methods of feeding, and sensitivity to pain/sedation. The CAS population is at high anaesthetic risk, and given their numerous operations, it will be important to track their mortality and morbidity. An important question to be addressed is: "Will early recognition and treatment of these infants improve their clinical and behavioral well being?"

Based on an incidence of 1/10,000, it is expected that 30-40 new cases per year will be diagnosed in Canada. As CAS presents with a wide spectrum of clinical severity, mildly affected patients may also be diagnosed and can be followed prospectively. The best way to study this population comprehensively will be to utilize a program such as the CPSP that raises physicians' awareness of conditions like CAS.

Duration

Fall 2001 to fall 2003

Reference

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Necrotizing fasciitis

“Relatively little information is known about the epidemiology of necrotizing fasciitis in Canadian children, a rare but potentially devastating life- and limb-threatening condition occurring either sporadically or in association with varicella.

Dr. H. Dele Davies

Necrotizing fasciitis (NF) is a deep-seated infection of the subcutaneous tissues resulting in progressive destruction of fascia and fat. This type of infection may or may not involve muscle (myositis). There are two types of NF: type I is due to mixed aerobic/anaerobic bacteria, while type II is due to group A streptococcus (GAS). Relatively little information is available in the literature on either types of NF. In Canada, most of the information has been derived from population-based studies in Ontario, consisting primarily of adults. In these studies, the risk of NF was estimated to be about one case per million population per year. In spite of the rarity of NF, its morbidity is substantial in the form of intensive care management, surgical interventions, including fasciotomies and amputations of body parts and a substanstial risk of death (10%).

Furthermore, this condition has captured the imagination of the media with the caption “flesh-eating disease” often appearing in headlines to describe persons affected. Evidence from the Ontario database suggests that varicella substantially increases the risk of invasive GAS infections including NF. For these reasons, and because of the other common illnesses caused by GAS, some investigators are in the process of examining vaccine candidates for GAS. Thus, it is important to capture the burden of illness in Canada for this disease to determine the national rates and outcome that will allow future repeat studies to see if such rates are impacted by vaccines. National surveillance through the CPSP will collect demographic information about the patients, presenting signs and symptoms, management and outcome that may provide clues to recognition, prognostication and economic impact.

Duration

Fall 2001 to fall 2003

Principal investigator

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International Developments

The International Network of Paediatric Surveillance Units (INoPSU) was established in 1998 to enhance collaboration between units from four continents, providing a unique opportunity for simultaneous cross-sectional studies of rare diseases in populations with diverse geographic and ethnic characteristics.

Currently worldwide, there are 11 national paediatric surveillance units. The population under surveillance includes 51 million children under the age of 15 years, with the assistance of over 8,500 clinicians who are asked each month to identify cases of rare or uncommon diseases in a childhood population. Participants in the Canadian Paediatric Surveillance Program (CPSP) represent 27.1% or 2,300 of these clinicians.

Financial support from Health Canada allowed the CPSP to invite INoPSU members to their first formal meeting in Ottawa in June 2000. *INoPSU 2000* was an unqualified success in accomplishing many of INoPSU's stated aims and benefits. Both the business meeting and scientific symposium, held in conjunction with the *Beyond 2000: Healthy Tomorrows for Children and Youth* conference, provided a welcomed opportunity for sharing information on the various methodologies of surveillance, study results, the increased awareness of the value of surveillance while recognizing potential confidentiality issues.

Joint collaborative studies are seen as an important method of advancing the knowledge of uncommon childhood disorders around the world. There are definite challenges. However, having an opportunity to meet colleagues and discuss practicalities and difficulties provides the stimulus to forge ahead.

It was agreed that INoPSU would apply for membership in the International Paediatric Association (IPA). An application will be presented to the IPA at their September 2001 meeting in Beijing.

TABLE 13

CPSP 2000 and 2001 studies under surveillance in other international units

Acute flaccid paralysis (AFP)	Australia, Netherlands, New Zealand, Papua New Guinea, Switzerland
Anaphylaxis (ANAP)	Britain
Cerebral edema in diabetic ketoacidosis (CE-DKA)	
CHARGE association/syndrome (CAS)	Australia
Congenital rubella syndrome (CRS)	Australia, Britain, New Zealand, Switzerland
Hemolytic uremic syndrome (HUS)	Australia, Britain, Latvia, New Zealand, Switzerland
Hemorrhagic disease of the newborn (HDNB)	Australia, Britain, Germany, Netherlands, New Zealand, Switzerland
Hepatitis C virus infection (HCV)	
Necrotizing fasciitis (NF)	
Neonatal herpes simplex virus infection (HSV)	Australia, New Zealand
Neonatal liver failure/perinatal hemochromatosis (NLF-PH)	
Progressive intellectual and neurological deterioration (PIND)	Britain
Smith-Lemli-Opitz syndrome (SLO)	
Subacute sclerosing panencephalitis (SSPE)	Britain, Papua New Guinea

Highlights from international units

Australia

Acute flaccid paralysis (AFP) has been under study by the Australian Paediatric Surveillance Unit (APSU) since March 1995 in response to the World Health Organization (WHO) requirement for active national surveillance in the process of accreditation of a region as polio-free. The expected incidence of AFP in Australia is one case per 100,000 children under the age of 15 years. The reported rate in April 2000 was 0.99 per 100,000 indicating that the surveillance system is sufficiently sensitive.

For the years 1995 to 1999, there were 143 cases of AFP with an additional 47 cases in 2000 after duplicates and errors were excluded. No cases of wild-type polio were identified to December 1999, and review by the National Polio Expert Committee is outstanding in 20 cases notified in 2000.

In addition to its contribution to certification of Australia as polio-free, the study has provided clinical data on the causes of AFP in Australian children. The most common diagnoses in non-polio AFP cases were Guillain-Barré syndrome (47%) and transverse myelitis (16%).

The highlight for the APSU in 2000 was the announcement by the WHO on October 29 that Australia, along with the other 36 countries of the Western Pacific region, is polio-free. The role of the APSU, in conjunction with the Victorian Infectious Diseases Research Laboratory and the Department of Health and Aged Care, has been crucial in this process. Surveillance for polio, using the APSU, must continue until there is global certification. The importance of the APSU and the AFP study was reinforced by both the WHO and the Federal government representatives at the Strategic Planning Meeting for Polio Eradication in Australia held in Canberra, in February 2001.

Britain

Active prospective surveillance of UK children with progressive intellectual and neurological deterioration (PIND) commenced in May 1997 and is expected to continue until April 2002. Funded by the Department of Health, this study is in collaboration with the National Creutzfeldt-Jakob Disease Surveillance Centre in Edinburgh and the Public Health Laboratory Service in London. The main aim of this surveillance is to gather unique epidemiological data on a variety of paediatric neurological conditions and to investigate whether UK children are developing variant Creutzfeldt-Jakob disease (vCJD). To mid-February 2001, a total of 1,086 children have been reported via the British Paediatric Surveillance Unit (BPSU). An expert group of six paediatric neurologists meets quarterly in London to classify the anonymous clinical information. They have discussed 785 cases and have allocated these to appropriate study groups as follows:
Group B – definite or probable vCJD = 4 cases (3 definite, 1 probable)
Group A – clear diagnosis, not vCJD = 435
Group U – meets case definition for PIND but still under investigation = 159
Group C – idiopathic PIND, not vCJD = 40
Not PIND (no case) = 147
227 cases are not included (e.g., reporting error, duplicate reports) and the remainder (74) are outstanding.

Four cases of vCJD (three definite and one probable) have been notified in the past 18 months — the youngest (ever reported) was a girl aged 12 years at onset. The other three were a girl aged 14 years and two boys aged 15 years at onset. Three have died and neuropathology has confirmed vCJD. As these four children were all notified relatively recently, the possibility remains that an increasing number of children will present with vCJD in the next year.

The study is producing unique national population-based data on the causes of PIND. The majority of children with PIND have a confirmed or likely

underlying diagnosis that is not vCJD. In the 435 children with a confirmed diagnosis there were 89 different neurodegenerative conditions. The six most commonly occurring diagnoses are the neuronal ceroid-lipofuscinoses (55 cases), the gangliosidoses (50 cases), mitochondrial encephalomyelopathies (38 cases), the mucopolysaccharidoses (33 cases), adrenoleukodystrophy (28 cases) and Niemann Pick Type C (22 cases).

Demographic analysis reveals interesting variations in reporting rates between paediatric centres. Yorkshire remains the region with the highest number of notifications (139). Paediatricians are still responding enthusiastically at an average rate of around 24 notifications per month.

Germany

Two major publications were based on the results of surveillance by the German Paediatric Surveillance Unit:

Schmitz T, von Kries R, Wist M, Schuster A. A nationwide survey in Germany on fatal asthma and near-fatal asthma in children: Different entities? Eur Respir J 2000; 16: 845-9

von Kries R, Siedler A, Schmitt HJ, Reinert RR. Proportion of invasive pneumococcal infections in children preventable by pneumococcal conjugate vaccines. Clin Infect Dis 2000; 31: 482-7

Latvia

Surveillance activities have been curtailed in Latvia due to personal health problems. Other complicating factors include the change in primary paediatric medical care organization to mostly family doctors, not more paediatricians. Only the hemolytic uremic syndrome study was continued with two cases in 2000.

Malaysia

Malaysia is a developing country with a developing paediatric surveillance unit. The program, established as part of the Malaysian Paediatric Association in 1994, is encountering problems of which funding is but one. The program has received some enquiries regarding studies but is awaiting decisions from the Malaysian Paediatric Association concerning the future of the program. In the interim, surveillance has been suspended.

Netherlands

The signal of pertussis in hospital was our program's highlight. The impact of this study influenced a change in our national vaccination policy. Instead of vaccinating at three, four, and five months, it was decided to vaccinate at two, three and four months, partly due to the found incidence of early cases of pertussis.

New Zealand

Seven confirmed cases of hemolytic uremic syndrome (HUS) in children were reported in 1999, compared to 14 cases in 1998. Information was not obtained on one notified case.

- The cases came from a geographically dispersed area, ranging from Auckland to Christchurch, although seven of the eight notified cases were from the North Island.
- The median age for the 1999 cohort of patients was 2.7 years, (range 0.3-14 years)
- In two cases, the Shiga toxin O157:H7 was detected in stool specimens. Two other infants developed HUS following pneumococcal meningitis.
- The mean of diagnosis was seven days (range 1-14 days).
- All children survived their initial disease but one infant was left with chronic renal failure following pneumococcal meningitis.

Although the rate of Shiga toxin-related infections continues to increase, the number of HUS cases has fallen in 1999. There are still delays in the diagnosis of this condition.

Papua New Guinea

Surveillance of renal tubular acidosis contributed to a publication, in collaboration with the University of Bristol and University College London, on the association of renal tubular acidosis with red cell ovalocytosis (Bruce LJ, Wrong O, Toye AM, Young MT, Ogle GD et al. J Biochem 2000; 350: 41-51).

This collaboration has led to improved management for Papua New Guinean children affected with renal tubular acidosis, as well as the academic interest.

Switzerland

In 1995, a new water-soluble mixed-micellar analogue of vitamin K_1 (Konakion® MM paediatric) was introduced in Switzerland to replace the formerly used fat-soluble Konakion® drops for the prevention of vitamin K_1 deficiency bleeding (VKDB) in infants. According to the new guidelines, an oral dose of 2 mg is given after birth and again on the fourth day of life. The impact of these guidelines on the incidence of VKDB was evaluated within the Swiss Paediatric Surveillance Unit (SPSU) from 1995 to 2000.

More than 99 % of infants received vitamin K_1 prophylaxis. Since July 1995, 93 % of the newborns have received prophylaxis according to the new guidelines; the remaining infants were given fat-soluble Konakion® drops or parenteral vitamin K_1. Within six years, one case of classical and 21 cases of late-onset VKDB (19 confirmed, two probable) were reported to the SPSU. Out of the 19 confirmed late-onset cases, 13 have received the recommended prophylaxis, whereas five have not and one had been given fat-soluble Konakion® drops. All but two confirmed cases of late-onset VKDB occurred in fully breast-fed infants and 14 of 19 had hepatobiliary disease.

The incidence of late-onset VKDB in infants who have received the recommended prophylaxis has decreased by 60% from 7.2:100,000 (95% CI 3.1-14.2) in 1986-1987 to 2.8:100,000 (95 % CI 1.1-5.8) between 1995 and 1998. Unfortunately, despite its better bioavailability, the mixed-micellar vitamin K_1 preparation does not protect all infants with underlying cholestatic disease. Our observations raise questions regarding the reported pharmacokinetics of Konakion® MM. It appears that absorption of this drug in infants with cholestasis is not as good as had been expected. This issue is the topic of a current detailed analysis of the data and review of the actual recommendations.

In summary, a mixed-micellar preparation of vitamin K_1 (Konakion® MM) is suitable for prophylaxis of VKDB in newborns and superior to the previously used fat-soluble preparation (Konakion®). However, the Swiss experience to date shows that a regimen consisting of two oral doses of Konakion® MM given during the first week of life does not protect all infants with cholestatic disease from late-onset VKDB. Oral prophylaxis in fully breastfed infants would have to include repetitive doses if protection from general prophylaxis is expected to include infants with hepatobiliary disease. Reference: Eur J Pediatr 1999; 148: 599-602

Wales

Surveillance of childhood tuberculosis in Wales was undertaken to measure the true incidence of childhood tuberculosis and to improve its control and management in Wales.

Objectives include: to establish an active surveillance system for childhood tuberculosis; to compile an accurate, detailed case register of childhood tuberculosis, including management and public health measures; to identify potential areas for improving prevention of tuberculosis; to remind clinicians of the importance of notification of tuberculosis and clear documentation of the diagnosis and management in the case notes; to improve knowledge of British Thoracic Society guidelines on tuberculosis.

Case definitions include: all cases of tuberculosis whether confirmed, probable or possible (as defined by the Public Health Laboratory Service) due to *Mycobacterium tuberculosis* complex in children from birth until and including the 16th birthday; pulmonary or extra pulmonary involvement and all children receiving chemoprophylaxis for tuberculosis. Infections due to atypical mycobacteria were excluded.

Twenty-nine cases of childhood tuberculosis (seven confirmed, 17 probable, five possible) and 38 children on chemoprophylaxis against tuberculosis have been reported to date. Two cases did not meet the criteria, one was an 18-year-old and the other was later confirmed by culture and reported as atypical mycobacteria. Site of tuberculosis: pulmonary, 12; lymph node extra-thoracic, four; lymph node intra-thoracic, seven; meningitis, three; abdominal, one and others, two.

Cases were seen predominantly in the white population. The majority of children had not had BCG vaccination, including several from the high-risk group. Among the 16 children belonging to ethnic minorities, seven had not been vaccinated with BCG, and the vaccination status was not known in two cases. In a number of cases, notification was incomplete or delayed. Three children were only given chemoprophylaxis even though the chest X-ray was abnormal. These should have been treated as possible cases. This is important because the duration of treatment is different. Two cases should have received chemoprophylaxis.

Childhood tuberculosis continues to be an important communicable disease problem. This is a reflection of the ongoing transmission of the disease in the population and also a measure of the effectiveness of the various preventive measures. The latter includes screening of new immigrants, detection and treatment of index cases, notification of index cases, contact tracing, chemoprophylaxis to susceptible contacts and BCG vaccination of the high-risk groups. The problem is compounded by undernotification of the disease and inconsistent adherence to published British Thoracic Society guidelines on tuberculosis.

TABLE 14

National paediatric surveillance units status circa end 2000

Country	Child population (10^6-aged 0-15 years)	Established	Respondents	Response rate
Australia	3.9	1992	942	95%
Britain/Eire	13.0	1986	2030	92%
Canada	6.3	1996	2294	82%
Germany	12.0	1992	460 *	98%
Latvia	0.4	1996	3	60%
Malaysia	7.6	1994	n/a	n/a
Netherlands	3.5	1992	448	85%
New Zealand	0.8	1997	165	92%
Papua New Guinea	1.8	1996	30	75%
Switzerland	1.3	1995	40 (38 clinics)	100%
Wales	0.6	1995	119	99.6%

* Heads of paediatric centres


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