
Investigation Into a Potential Neurological Syndrome of Unknown Cause

FINAL REPORT

February 24, 2022

Public Health New Brunswick

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Acronyms

FEDERAL ORGANIZATIONS

CJDSS	Creutzfeldt-Jakob Disease Surveillance System (PHAC)
CFEZID	Centre for Food-borne, Environmental and Zoonotic Infectious Diseases (PHAC)
CFIA	Canadian Food Inspection Agency
CNPHI	Canadian Network for Public Health Intelligence
NML	National Microbiology Laboratory (PHAC)
PHAC	Public Health Agency of Canada (PHAC)
OMD	Outbreak Management Division (PHAC)
CFEP	Canadian Field Epidemiology Program (PHAC)

PROVINCIAL ORGANIZATIONS

DAAF	Department of Agriculture, Aquaculture and Fisheries (GNB)
DELG	Department of Environment and Local Government (GNB)
DNRED	Department of Natural Resources and Energy Development (GNB)
DH	Department of Health (GNB)
GNB	Government of New Brunswick
HHN	Horizon Health Network
MIND Clinic	Moncton Interdisciplinary Neurodegenerative Diseases Clinic (HHN)
PHNB	Public Health New Brunswick (GNB)
BCCDC	British Columbia Centre for Disease Control
VHN	Vitalité Health Network

NON-GOVERNMENT ORGANIZATIONS

CCWC	Canadian Wildlife Health Cooperative
CIHR	Canadian Institute for Health Research
NRC	National Research Council
UBC	University of British Columbia

Highlights

New Brunswick healthcare providers play a critical role in the early detection of clusters and outbreaks of disease. Continued support of this collaborative approach between physicians and Public Health New Brunswick (PHNB) is necessary for timely outbreak investigations.

The PHNB investigation of a neurological syndrome of unknown cause, including the *Epidemiological Summary of Enhanced Surveillance Interviews* and the *Oversight Committee Report*, concludes there is no evidence of a cluster of neurological syndrome of unknown cause.

Neurological conditions can be very difficult to diagnose and it is frequently the case that individuals exhibit less common presentations of known diseases; however, findings from the detailed review of the reported cases by the Oversight Committee found that the people who were part of this cluster displayed symptoms that varied significantly from case to case and there was no evidence of a shared common illness or of a syndrome of unknown cause. No individual met the case definition established by the main referring physician and the Creutzfeldt-Jakob Disease Surveillance System (CJDSS). Additionally, extensive interviews conducted with the suspect cases or their proxies did not identify any specific behaviours, foods, or environmental exposures that can be identified as potential risk factors.

PHNB is therefore concluding its investigation into a neurological syndrome of unknown cause and recommends that patients who were advised they may have a neurological syndrome of unknown cause contact their primary care provider for a referral to seek treatment and care at the Moncton Interdisciplinary Neurodegenerative Diseases (MIND) Clinic or with another specialist physician.

Privacy Statement

When disclosing information, Public Health New Brunswick (PHNB) always:

- respects the imperative need to find the right balance between the public's need and right to know, and the duty to protect the privacy of all New Brunswickers
- follows the principle of necessity and proportionality: information is disclosed in a manner that does not permit the identification of affected individuals but is sufficient to fully inform the public

The findings presented in this report follow applicable privacy legislation, including the *Personal Health Information Privacy and Access Act* (PHIPAA), the *Right to Information and Protection of Privacy Act* (RTIPPA), as well as best practices to ensure every individual's right to privacy is protected at all times.

Some of the information used for this investigation was collected directly from individuals, who provided their informed consent, which included assurance that no personal or identifying information would be disclosed in the report of findings.

Acknowledgements

While reflecting on the findings presented in this report, we are reminded that it is those affected and the people who love them who are at the heart of any public health investigation.

Neurodegenerative diseases are debilitating illnesses which affect individuals, families, and communities. The individuals who were identified as being part of a cluster of a neurological syndrome of unknown cause have undergone much hardship, exacerbated by various commentators engaging in unfounded public speculation, posing unanswered questions, and arriving at premature conclusions. Despite this, individuals gave generously of their time and insights, which helped guide the direction of the investigation.

Health-care professionals, including physicians and their supporting staff, play a vital role in public health as they are often the first to see emerging threats to our health and safety. We rely on these professionals to be vigilant in the identification and treatment of diseases. It is essential that we continue to support them in these endeavors.

We would like to thank those collaborators from across the country who responded to our call to action and came together as a multidisciplinary team of experts. That expertise helped Public Health New Brunswick discern plausible hypotheses, build investigation tools, and inform investigation activities.

PHNB is particularly appreciative of our partnership with the Public Health Agency of Canada (PHAC) and our continued collaboration to modernize and improve the processes for supporting the health and wellbeing of our citizens.

PHNB is extremely grateful to the members of the Oversight Committee, in particular the Co-chairs who led the work of the committee and the six neurologists who gave tirelessly of their considerable expertise despite carrying extremely large and challenging caseloads during their normal functions. It is through their efforts that the individuals in the cluster and their families are able to move closer to receiving the answers they seek.

Another large debt of gratitude is owed to the Moncton Interdisciplinary Neurodegenerative Diseases (MIND) Clinic, which, throughout this process, provided and will continue to provide coordinated care and support to affected individuals and their families. In addition to the collaborative, team-based medical services they provide on a daily basis, the MIND Clinic's support and research staff made direct contributions to the progress of this investigation by liaising with the affected individuals and facilitating PHNB's timely access to information. Their assistance was invaluable.

A special note of appreciation also goes to the public health nurses who assisted with and conducted the enhanced surveillance interviews. Their work was integral to this process.

Lastly and most importantly, to the individuals who were part of this investigation and their families, PHNB heartily thanks you for your participation. We sincerely hope that the findings of this investigation will provide you with a clearer path as you move forward and we remain committed to ensuring you receive the care, help, and support you require.

Overview

Amid a global pandemic, an identified cluster of individuals in New Brunswick with a potential neurological syndrome of unknown cause, and the public health investigation looking into it, have garnered considerable local and international attention. The possibility of suffering from a fast acting, debilitating, and potentially fatal illness with an unknown cause is a truly frightening prospect. To better understand the identified condition, ensure the health and safety of the public and provide appropriate care to the affected individuals, PHNB and its collaborators have been investigating this potential neurological syndrome.

NEURODEGENERATIVE DISORDERS

Neurodegenerative disorders, including dementia, are one of the leading causes of disability affecting Canadians. These disorders can be severe enough to impact daily living, independence, and relationships. Neurodegenerative disorders are caused by many diseases, injuries, and conditions that affect the central nervous system and different parts of the brain. They are characterized by the steady loss of neurons in the brain or spinal cord that result in diseases or conditions that lead to progressive deterioration of cognitive functions and motor abilities. These include dementias, Alzheimer's disease, Parkinson's disease, multiple sclerosis, amyotrophic lateral sclerosis (also known as ALS or Lou Gehrig's disease), Huntington's disease, and a large number of rarer diseases like Wilson's disease or Creutzfeldt-Jakob disease (CJD).

CREUTZFELDT-JACOB DISEASE

Creutzfeldt-Jakob Disease is a rare, fatal, degenerative brain disorder caused by an infectious protein or prion. The Canadian Creutzfeldt-Jakob Disease Surveillance System (CJDSS) is operated by PHAC and provides national surveillance for all types of human prion diseases in Canada. Physicians and other health-care providers maintain awareness of CJD and provide patient referrals to the CJDSS for full case investigation. The CJDSS contributes to this collaborative process by providing laboratory testing services, clinical coordination, expert consultation and logistic support, all of which facilitate diagnostic investigation for CJD and prion diseases.

The CJDSS case investigation of patient referrals from Canadian physicians classifies the referral as either not a case of CJD; or as a possible, probable, or definite case of CJD (national surveillance case definition). All human prion diseases are provincially or territorially reportable and nationally notifiable in Canada. The CJDSS assumes responsibility for national notification, however it is the legal responsibility of the diagnosing health-care provider to report definite, probable and possible cases of CJD (national surveillance case definitions) to their local authorities, in this case, the PHNB.

THE PUBLIC HEALTH ACT

The New Brunswick *Public Health Act* and its seven regulations is meant to help protect the public from health hazards, environmental risks and communicable diseases. These constitute the legal authority of the Department of Health (DH) and PHNB for the management (surveillance, investigation, prevention, and control) of notifiable diseases and events in New Brunswick. Diseases like CJD, *Escherichia coli* infection, tuberculosis, legionella and measles, and associated clusters or outbreaks of disease as well as unusual illness are required to be reported to PHNB.

THE PHNB INVESTIGATION

In early 2020, the CJDSS experienced an unusual increase in the number of patients being referred for CJD case investigation by New Brunswick physicians, and the increase continued throughout the year. During a September 30 meeting with PHNB, the CJDSS provided information about the increased number of CJD patient referrals being made to them and described the cases as having atypical, rapidly progressive dementia. PHNB did not receive detailed reports for any of these cases from the referring physicians. It was later determined that the referrals were not evenly distributed, coming mainly from one region of the Province as 46 of these cases were referred by a single neurologist.

In December, additional information provided by the CJDSS indicated that some of the patients had been investigated by the CJDSS and were not considered cases of CJD or other known prion diseases. The CJDSS was concerned that the individuals were part of a cluster (or group) with a neurological syndrome of unknown cause (etiology) and provided an initial draft case definition. Detailed case information was not made available to PHNB from the primary neurologist involved in the referrals or the CJDSS at this juncture.

An essential component of PHNB's mandate is to investigate clusters, disease outbreaks or other threats when they emerge to protect the health of the people of New Brunswick. Public Health New Brunswick can receive information about potential threats to the public from numerous sources, including the public, media, clinicians, and other parts of the health system.

PHNB investigators search for the cause, identify people who are at risk, and determine how to control or stop the spread or prevent it from happening again. They systematically gather information, asking questions such as: Who is sick? What are their symptoms? When did they get sick? What is causing them to be sick? Where could they have been exposed? Outbreak investigations require a lot of time and energy to find out what is making people sick. Using critical thinking, reasoning skills, epidemiological methods and statistical analysis, there is a rigorous assessment and ongoing interpretation of evidence and information from multiple sources throughout the investigation to answer the questions. Some investigations into clusters turn out to be true outbreaks with a common cause, some are sporadic and unrelated cases of the same disease, and others are unrelated cases with similar presentations but unrelated causes or diseases.

Surveillance case definitions are developed early in an outbreak investigation. Surveillance case definitions standardize criteria and help identify people who are at risk and are used for classification of cases. Without a known disease and with the patients investigated determined not to be a case of CJD by the CJDSS, the clinical signs and symptoms being exhibited by the patients were the criteria used for identifying cases to be included in the cluster. On January 29, 2021, the case definition for the progressive neurological syndrome of unknown etiology was revised to include additional surveillance criteria.

Following the development of the case definition (Appendix A), the CJDSS shared preliminary data with PHNB. Collaboration continued between PHNB and CJDSS on further investigation steps and processes. Two field epidemiologists from the Canadian Field Epidemiology Program (CFEP) also provided additional support to PHNB at this juncture of the investigation until more surveillance staff were onboarded provincially.

Although the data was limited to information collected through the routine surveillance of prion diseases, it indicated that most of the cases had been referred to the CJDSS within the last few years and that they were located in the same geographic areas. At the time of referral, most of the individuals were living in the southeastern and northeastern regions of New Brunswick, around the Moncton area and the Acadian Peninsula. These characteristics suggested that the cluster could be associated with a common source exposure; however, additional information not yet collected by the parties involved was needed to properly characterize the cases and identify potential causes and sources. It was later revealed to be a result of the zones where services are

provided by the Vitalité Health Network (VHN), and within which the primary referring neurologist operates. PHNB made repeated requests to the main referring physician for more detailed clinical case information on each of the individuals identified by them but were unfortunately not able to obtain the information.

Out of an abundance of caution and to help identify other individuals in New Brunswick who could be part of the cluster, a memo was issued on March 5, 2021 to provincial health-care professionals to advise them of the cluster of cases with a potential progressive neurological syndrome of unknown etiology (Appendix B). Health-care providers concerned about CJD being a cause of a patient's clinical illness would continue, as usual, to refer patients to the CJDSS.

To help identify individuals in Canada and other countries who could be part of the cluster, on March 19, 2021, PHNB posted an alert on the Canadian Network for Public Health Intelligence (CNPHI) that informed public health officials across Canada of the investigation and advised them to contact Public Health New Brunswick for further information. The Public Health Agency of Canada had been in contact with other countries to provide further information and asked to be notified if potential cases were identified outside of Canada. To date, no cases of individuals with the neurological syndrome of unknown cause have been identified outside of New Brunswick.

The DH webpage was launched May 2021 to provide an overview of the province's investigation into the cause of the potential syndrome, its possible symptoms and the possible cases identified. The webpage was periodically updated as the investigation progressed.

The Horizon Health Network (HHN) and DH also announced funding in April 2021 for a special neurodegenerative disorder clinic to provide better support for patients with rapid or early-onset cognitive decline, which became the MIND Clinic. Initially set-up to provide additional nursing and administrative support to the main referring physician, the MIND Clinic has grown significantly and the team currently consists of two geriatricians, two neurologists, a registered nurse, a neuropsychologist, a social worker, a research manager, and an administrative assistant. There is also an associate neurologist and an associate psychiatrist.

A memo was issued on October 26, 2021 to health-care professionals in New Brunswick advising that patients who met the case definition should be referred directly to the MIND Clinic (Appendix C). Referrals would be assessed by specialists working with the MIND Clinic to confirm a clinical diagnosis, initiate appropriate treatment, and identify additional cases. To ensure proper inclusion of cases in this cluster, the addition of new patients would now require the consensus of two specialty physicians.

Collaborations between PHNB and federal partners, provincial or territorial jurisdictions, and other experts is a frequent occurrence in outbreak investigations, which routinely use a multidisciplinary approach.

During the course of this investigation, PHNB regularly consulted with the main referring physician and medical officers of health, and with provincial and federal partners including:

- Agriculture, Aquaculture and Fisheries (DAAF)
- Environment and Local Government (DELG)
- Natural Resources and Energy Development (DNRED)
- The Canadian Food Inspection Agency (CFIA)
- The Public Health Agency of Canada (PHAC), including:
 - The Canadian Field Epidemiology Program (CFEP)
 - The Centre for Food-borne, Environmental, and Zoonotic Infectious Diseases (CFEZID)

- The Outbreak Management Division (OMD)
- The Policy Integration and Zoonoses Division
- CJDSS
- The National Microbiology Laboratory (NML)

Additional consultation occurred with experts from:

- The British Columbia Centre for Disease Control (BCCDC)
- The Canadian Institutes for Health Research (CIHR)
- The Canadian Wildlife Health Cooperative (CWHC)
- The National Research Council (NRC)
- The University of British Columbia (UBC)

PHNB consolidated the various ongoing consultations with provincial and federal partners into a single multidisciplinary team and held weekly meetings beginning on March 25, 2021. The multidisciplinary team members provided the broad and comprehensive expertise needed to inform the investigation; additional subject matter experts were consulted as necessary.

The most effective way to generate a hypothesis on the likely cause of an outbreak is to identify common exposures among cases by interviewing cases using a surveillance questionnaire and analyzing identified exposures. While providing expertise and guidance for the questionnaire, the multidisciplinary team considered hypotheses that could be a potential cause based on historical information, current research, and expert opinion. Hypothesis generation is a challenging part of outbreak investigation and is an ongoing process.

The possible explanations are re-evaluated as new information is acquired through the investigation and may become more likely or less likely according to the observed evidence. Once a hypothesis is considered to be a possible cause, the investigators consider the evidence and determine what additional actions are required. For example, if three different food items are possible causes, the food samples could be tested for a pathogen or toxin.

The multidisciplinary team discussed many potential hypotheses that could possibly explain a cluster of a potential progressive neurological syndrome. However, there was insufficient scientific evidence to consider any one hypothesis as a likely cause. In light of this, the team considered actions that could be undertaken until additional evidence from the epidemiological analysis of surveillance interview responses became available. These actions included sample collection for blue-green algae (cyanobacteria) and Chronic Wasting Disease (CWD) and collaborating with the Canadian Food Inspection Agency (CFIA) on the Canadian Shellfish Sanitation Program (CSSP).

The Department of Environment and Local Government (DELG) and Department of Health (DH) provide surveillance for harmful algae blooms which may be present in freshwater bodies in the province. When algal blooms are reported in the province samples are collected and analyzed to determine the type and concentration of algae present, including blue-green algae (cyanobacteria), blue-green algae advisories are then issued accordingly. During 2021, DELG agreed to collect additional samples from water bodies with blue-green algae blooms in case further analysis was warranted; however, the conditions that produce algae blooms were not present in that year and no algae blooms were observed during the warmer summer months; additional sampling did not occur.

CWD is a prion disease that affects white-tailed deer; however, there has been no known transmission of CWD to humans to date. The CFIA, DH, DNRED, and DAAF agreed to collect and test deer from New Brunswick for CWD. The focus was to collect, and test mature deer killed as a result of vehicle collision. The survey started in fall 2021 and ended in January 2022. The results were not available in time for inclusion in this report but will be available at a later date. However, the findings of the *Epidemiological Summary of Enhanced Surveillance Interviews* did not provide any evidence that the consumption of cervid meat as a potential exposure to CWD would be a potential risk factor to the individuals identified in this cluster.

The Canadian Food Inspection Agency (CFIA), Environment and Climate Change Canada (ECCC) and Fisheries and Oceans Canada (DFO) jointly administer the Canadian Shellfish Sanitation Program (CSSP), a federal food safety program whose goal is to minimize the health risks associated with the consumption of contaminated bivalve molluscan shellfish such as mussels, oysters and clams. Under the CSSP, the Government of Canada implements controls to verify that only shellfish that meet food safety and quality standards reach domestic and international markets. PHNB collaborated with CFIA on shellfish surveillance and there was no significant evidence that identified shellfish as a potential risk factor in this investigation.

THE EPIDEMIOLOGICAL SURVEILLANCE SURVEY

The expertise and collaborations of the multidisciplinary team members were influential in guiding the investigation on its next steps. The surveillance questionnaire was developed in collaboration with the multidisciplinary team, Outbreak Management Division (OMD), and PHNB. The questionnaire would be administered through telephone interviews with the cases or their representatives, who generously took the time to complete it, and would solicit input to identify any commonalities among the cases and help answer how and where people were potentially becoming exposed.

The questionnaire included:

- demographic information
- background information (e.g. where people lived and travelled)
- food exposure information (e.g. eating fish, wild game, fiddleheads or shellfish)
- environmental exposure information (i.e. Animals, industrial and recreational water exposures)
- and information on activities related to work, volunteering, or hobbies

The intent of the epidemiological analysis of the surveillance questionnaire responses was to provide the necessary information for additional hypothesis generation and further testing.

Starting in May 2021, the interviews were conducted by bilingual Public Health nurses trained and experienced in outbreak investigation and patient interviews. The questionnaire focused on broad initial questions which might be further refined through subsequent inquiries. The questionnaire was administered through lengthy interview sessions, which took an average of four hours. The responses were analyzed using a comprehensive approach involving quantitative and qualitative methods.

The process of conducting the epidemiological survey took more time than anticipated, due to the difficulties PHNB experienced in obtaining the names and contact information from the main referring neurologist. Despite repeated requests for this information starting in mid-April 2021, the last of the information was not provided to PHNB until early August 2021 and it did not include contact information on the entire 48 individuals. PHAC ultimately provided the contact information required to complete the interviews at the end of July.

In May 2021, the multidisciplinary team meetings were paused until additional information from the surveillance questionnaire and the oversight committee review became available. These results would inform the need for the resumption of meetings and further investigations, including directions for research, testing and sampling.

The analysis of the interview responses was released in the report *Investigation into a Neurological Syndrome of Unknown Cause: An Epidemiological Summary of Enhanced Surveillance Interviews* on October 26, 2021. This report concluded that there were no specific commonalities related to behaviours, foods, geographic regions, or environmental factors that could have been a potential cause or source associated with the neurological syndrome of unknown cause.

THE OVERSIGHT COMMITTEE AND CASE REVIEWS

On June 2, 2021, PHNB announced the creation of an independent oversight committee, which was tasked with providing peer review and expert oversight of the identified cases, ensuring due diligence and helping to determine if there were potential alternative diagnoses or if more investigation is indicated. This work involved, but was not limited to, a comprehensive review of clinical and diagnostic records and information.

Due to difficulties in accessing the medical records of patients included in the cluster, the first case reviews were not assigned until the beginning of August 2021. Despite multiple attempts, PHNB was not able to obtain the needed information from the main referring neurologist. Compounding this, in New Brunswick, individual medical records are contained within various systems that are set up to protect the privacy rights and personal and medical information of its citizens. PHNB does not have access to these records and, as a result, had to seek special approvals for the purpose of conducting this investigation.

The role of the neurologists on this committee was to provide peer reviews and independent expert oversight of the identified cases, to ensure due diligence and help determine if there were potential alternative diagnoses. This work included but was not limited to a comprehensive review of clinical and diagnostic records and information including patient's demographic information, presenting complaints, past medical history, social history, family history, treatment history, examination history, and other medical investigations.

Between August 2021 and February 2022, the Oversight Committee conducted full case reviews, including chart reviews and secondary reviews, for the 48 individuals identified as members of the cluster as of April 30, 2021. Individuals were identified based on clinical presentation as determined by the main referring neurologist. During the in-depth clinical reviews, cases were randomly allocated to pairs of neurologists, who reviewed independently and then presented and discussed their findings with the full committee consisting of six neurologists, co-chairs from HHN and VHN, and a Medical Officer of Health acting as a liaison with PHNB.

Once the reviews were completed, the Oversight Committee sent letters to the individuals' primary care physicians with its conclusions around whether an individual should be included or excluded from the cluster and to provide recommendations for follow-up testing and treatment, as applicable. They also communicated their findings directly with patients or their families.

During the course of this investigation, the Department of Health was asked by individuals to include a patient advocate on the Oversight Committee. As the committee was reviewing personal health information, this request could not be accommodated due to legal obligations to protect an individual's privacy. However, we recognize that the lack of engagement often left patients feeling abandoned despite all the investigation work being completed by medical personnel and public health officials.

OVERSIGHT COMMITTEE FINDINGS

On February 22, 2022, the Oversight Committee presented its findings to the DH. The committee unanimously found that none of the cases fulfilled the full criteria of the case definition.

After completing the review of records, neurologists provided potential alternative diagnoses for 41 patients (85%). The alternate diagnoses provided included some known conditions like Alzheimer's disease, Lewy body dementia, mixed dementia, diabetic or inflammatory polyneuropathy, Parkinson disease dementia, fronto-temporal dementia, alcohol related cerebellar dysfunction, post-concussion syndrome, chronic traumatic encephalopathy, paranoid schizophrenia, chronic Fatigue Syndrome, Chronic severe anxiety disorder, and cancer. In addition, for the ten patients who are deceased, diagnoses have been confirmed by autopsy or by the review of medical records and has provided sufficient evidence of an alternative diagnosis.

Furthermore, out of the 48 cases, none fulfilled the full criteria of the case definition. Only twenty-five out of 48 cases met the criteria for rapidly progressing dementia. Only 19 of those had at least four of the clinical features mentioned in the definition, which were verified directly by a physician. Out of those 19 cases, one case did not manifest those symptoms during the first 18-36 months of illness. One other case did not fulfill the criteria for supporting investigations (in MRI, EEG, and SPECT-CT) as an alternative diagnosis was provided. There was no evidence of a known prion disease in any of these cases. In the remaining 17 cases there was sufficient evidence for alternative diagnoses (or potential alternative diagnoses). The findings are shown in Table 1.

The committee concluded that although some of the cases had presentations with unusual symptomology, they do not have a common illness with an unknown etiology and there is no evidence of a cluster of a neurological syndrome of unknown cause.

Table 1: Summary of Case Definition Analysis

Case Definition Criteria	Cases = 48
Number of cases meeting the full case definition	0 (0%)
Number of cases with rapidly progressing dementia (within 2 years)	25 (52%)
Number of cases with clinical features manifesting within 3 years	19 (40%)
Number of cases presenting with at least 4 clinical features	18 (38%)
Number of cases with one or more findings supporting investigation	17 (35%)
Number of cases with suggested alternative diagnoses/diagnoses	17 (35%)

Conclusion

Many hypotheses and theories have been shared publicly surrounding this cluster of a potential neurological syndrome of unknown cause since it was first identified. Unfortunately, many of the theories which caught people's attention were based on speculation, uncorroborated opinions and in the absence of a thorough analysis of epidemiological and clinical information. The result of this has been undue stress and anxiety for patients and their families dealing with this illness as well as a perceived threat to the health of the general population. The investigation led by Public Health New Brunswick with the assistance of many provincial and federal partners was designed to provide an independent evidence- and scientific-based assessment of this potential outbreak and to identify the associated health risks to the population of New Brunswick.

The PHNB investigation of a potential neurological syndrome of unknown cause, including the *Epidemiological Summary of Enhanced Surveillance Interviews* and the *Oversight Committee Report*, concludes there is no evidence of such a cluster and that there are no specific behaviours, foods, or environmental exposures that can be identified as potential risk factors. Based on the fact that 48 out of 48 individuals did not meet the case definition, supported by the 10 deceased individuals all having an alternative diagnosis, 6 of which were confirmed by autopsy, there is no evidence of an unknown neurological illness. PHNB is therefore ending the investigation into a potential neurological syndrome of unknown cause.

Diagnosing neurodegenerative illnesses is a complicated matter and sometimes can take years to achieve. This review has highlighted the need, before any individual is presumed to have an unknown neurological condition, for the referring physician to seek a second opinion. Not only is this best medical practice, but it addresses the issue of potential physician bias. This could have alleviated a lot of stress and uncertainty faced by those included in the cluster. This is particularly true in light of information that the CJDSS has shared with PHNB regarding the fact that the referring physician had also informed them that five cases were to be removed from the cluster due to another diagnosis being identified for those patients.

Neurological conditions can be very difficult to diagnose and it is frequently the case that individuals exhibit less common presentations of known diseases. However, the individuals being investigated within this cluster displayed symptoms that varied significantly from case to case and there was no evidence of a shared common illness or of a potential syndrome of unknown cause. Furthermore, neuropathology findings for all deceased patients who have undergone an autopsy confirm a diagnosis of known conditions, such as Alzheimer's disease, Lewy body disease, or cancer.

This investigation has highlighted areas of improvement and issues that need to be addressed in order to avoid people going through this kind of hardship in the future. To this end, PHNB is including recommendations in this report to address the gaps in the process.

Although there is no evidence of a cluster with a neurological syndrome of unknown cause, we acknowledge that individuals continue to experience symptoms that affect their daily lives. Being diagnosed with or suspecting you or a loved one have a neurodegenerative disorder is extremely distressing, particularly if it has also been described as an unknown disease. PHNB recommends that all patients who were advised they may have a neurological syndrome of unknown cause or who may have a neurodegenerative disorder, contact their primary care provider for a referral to seek further treatment and care at the Moncton Interdisciplinary Neurodegenerative Diseases (MIND) Clinic. The MIND Clinic is a cross-specialty collaborative precision medicine clinic for neurocognitive disorders affecting adult patients of any age. Their primary goal is to assess, diagnose, and provide ongoing care and treatment to patients with progressive neurodegenerative diseases to improve

their quality of life, and provide family support. Referrals from primary care providers are accepted from within New Brunswick for adults of any age with progressive neurocognitive symptoms.

Recommendations

- The possibility of suffering from a fast acting, debilitating and potentially fatal illness with an unknown cause is a truly frightening prospect. In retrospect, it is clear the website communications and press releases did not adequately address this anxiety or provide support to patients and their families. Public Health should complete a review of its communication and patient engagement practices during investigations to improve in this area.
- Risk communication requires planning, preparation, and practice to be effective. Communication strategies that better address public concerns in such events should be considered by the Department of Health. For example, providing a spokesperson, public or individual meetings or phone calls, or letters to affected people.
- Upon the discovery of a potential neurological syndrome of unknown cause, the DH funded the creation of a centre for care of adults with neurocognitive disorders, which includes an associated research program. The MIND Clinic should continue to provide coordinated care, including diagnoses and treatment options, to patients being investigated for neurodegenerative diseases.
- The government of New Brunswick, in collaboration with HHN and the VHN, should pursue research funding from national granting agencies, such as the Canadian Institutes of Health Research, to help continue to advance research initiatives in neurosciences in the province of New Brunswick.
- PHNB should continue to ensure early involvement of clinicians, specialty medical departments, and regional health authorities in a cluster or outbreak investigation of an unknown illness characterized only by clinical symptoms to validate the conclusions of referring physicians. In the future, PHNB may request a clinical review of cases by a second specialist physician prior to inclusion of cases into a cluster of unknown etiology. If no consensus can be reached, the case should be presented to a board of specialty doctors or an oversight committee for determination.
- Enhance the *Reporting and Diseases Regulation* 2009-136 under the *Public Health Act* (O.C. 2009-455) by including the addition of suspect case of any existing or new variant of human or animal prion disease as a Part 3 notifiable event to remove any ambiguity on the necessity to report any such instances to provincial public health officials.
- PHNB should continue ongoing collaborations with NB physicians and health care practitioners to improve provincial surveillance and reporting of notifiable diseases and events.
- PHNB should continue to build on collaborations with PHAC and other federal and provincial partners to improve and modernize the national CJD surveillance system and to establish or improve processes related to outbreak investigations, including those where prion disease has been excluded. To this end, PHNB would support the creation of Federal, Provincial and Territorial working group that would support this review.
- PHNB will continue to engage PHAC in the development of national surveillance tools, including national surveillance questionnaires and data dictionaries, to ensure consistency of data interpretation across jurisdictions.
- Data sharing agreements between PHNB and the regional health authorities should be created and clearly outline the administrative processes required to ensure timely access to clinical information during outbreak investigations.

- The Oversight Committee has made additional recommendations with regards to the creation of protocols for the sharing of medical records subject to an outbreak investigation as well as the continued care of individuals involved in this investigation. PHNB agrees with and supports these recommendations.

Appendix A – Case definition

CONFIRMED CASE

Progressive neurological syndrome involving rapidly progressing dementia and at least four of the following clinical features, verified directly where possible by a physician:

- Cerebellar ataxia (gait ataxia, truncal ataxia, cerebellar dysarthria or dysmetria), abnormal cerebellar function test or cerebellar symptoms (dysdiadochokinesis, intention tremor etc.)
- Psychiatric symptoms (agitation/irritability, aggressiveness, apathy/withdrawal, anxiety or obsessive behaviour)
- Visual hallucinations, cortical blindness or other cortical visual symptoms
- Pyramidal or extrapyramidal signs, including atypical Parkinsonism
- Myoclonus
- Painful sensory symptoms (limb pain, dysesthesia or paresthesia) persisting for six months or more, in absence of peripheral nervous system dysfunction
- Muscle atrophy

The majority of these should manifest during the first 18 to 36 months of illness

AND

One or more of the following findings from supporting investigations:

- Atrophy, greater than expected for age on MRI
- EEG slowing or hypoperfusion on SPECT (CT) or hypometabolism on PET-CT scan

AND

Insufficient evidence for an alternative diagnosis, including known forms of human prion disease

SUSPECT CASE

Progressive neurological syndrome involving at least four of the following clinical features, verified directly where possible by a health care provider:

- Rapidly progressing dementia
- Cerebellar ataxia (gait ataxia, truncal ataxia, cerebellar dysarthria or dysmetria), abnormal cerebellar function test or cerebellar symptoms (dysdiadochokinesis, intention tremor etc.)
- Psychiatric symptoms (agitation/irritability, aggressiveness, apathy/withdrawal, anxiety or obsessive behaviour)
- Visual hallucinations, cortical blindness or other cortical visual symptoms
- Pyramidal or extrapyramidal signs, including atypical Parkinsonism
- Myoclonus
- Painful sensory symptoms (limb pain, dysesthesia or paresthesia) persisting for six months or more, in absence of peripheral nervous system dysfunction
- Muscle atrophy

The majority of these should manifest during the first 18 to 36 months of illness.

AND

Insufficient evidence for an alternative diagnosis.

Appendix B – March 5, 2021 Memo



Memo Note

Department of Health / Ministère de la Santé
Office of the Chief Medical Officer of Health /
Bureau du médecin-hygiéniste en chef
P.O. Box/C.P. 5100
Fredericton, NB E3B 5G8
Tel/Tél. (506) 457-4800
Fax/Télé. (506) 453-2780

Date : March 5, 2021 / Le 5 mars 2021

To/Dest. : Health care professionals, NBMS, NANB, NBPA, College of Pharmacists, LPN Association, RHAs (PH and clinical) / Professionnels de la santé, SMNB, AINB, APNB, Ordre des pharmaciens, Association des infirmières et infirmiers du Nouveau-Brunswick (SP et clinique)

From/Exp. : Dr. / D^{re} Cristin Muecke, Deputy Chief Medical Officer of Health / Médecin-hygiéniste en chef adjointe

Copies : Dr. / D^{re} Jennifer Russell; RMOHs / MHR; Heidi Liston, Jeff McCarthy, Penny Higdon, Shelley Landsburg, Hanan Smadi, NBHEOC / COUMSNB, Nina van der Pluijm, Dr./D^{re} Alier Marrero

Subject/Objet : **Cluster of Progressive Neurological Syndrome of Unknown Etiology in New Brunswick, Canada / Grappe de cas du syndrome neurologique progressif d'étiologie inconnue au Nouveau-Brunswick, Canada**

Public Health New Brunswick wishes to make you aware of a cluster of progressive neurological syndrome of unknown etiology in the province. To date in New Brunswick, there have been 40 cases referred to the national Creutzfeldt Jakob Disease Surveillance System (CJDSS) as part of this cluster under investigation: 1 case in 2015 (retrospectively identified), 11 cases in 2019, 24 cases in 2020, and 4 cases thus far in 2021. Five cases (13%) have died; all met the case definition for a confirmed case of this syndrome (see Appendix 1 for case definition and Appendix 2 for Epi Curve).

Preliminary investigation conducted in late 2019/early 2020 determined this to be a distinct atypical neurological syndrome. While these cases have many similarities to Creutzfeldt Jacob Disease (CJD), testing for CJD so far has ruled out known prion diseases. We are collaborating with different national groups and experts; however, no clear cause has been identified at this time.

Santé publique Nouveau-Brunswick souhaite vous informer d'une grappe de cas d'un syndrome neurologique progressif d'étiologie inconnue dans la province. À ce jour, au Nouveau-Brunswick, 40 cas ont été signalés au Système de surveillance de la maladie de Creutzfeldt-Jakob (SSMCJ) canadien dans le cadre de l'enquête portant sur ces cas : 1 cas en 2015 (diagnostiqué rétrospectivement), 11 cas en 2019, 24 cas en 2020, et 4 cas jusqu'à présent en 2021. Cinq cas (13 %) sont décédés; tous répondaient à la définition de cas pour un cas confirmé du syndrome (voir l'annexe 1 pour la définition de cas et l'annexe 2 pour la courbe épidémiologique).

L'enquête préliminaire menée à la fin de 2019 et au début de 2020 a déterminé qu'il s'agissait d'un syndrome neurologique atypique distinct. Bien que ces cas présentent de nombreuses similitudes avec la maladie de Creutzfeldt-Jacob (MCJ), les tests de dépistage de la MCJ ont jusqu'à présent écarté les maladies à prion connues. Nous collaborons avec différents groupes et experts nationaux; cependant, aucune cause précise n'a été déterminée à ce jour.

Overall cases are equally distributed among males (n=20, 50%) and females (n=20, 50%). The median age is 59 years. Approximately, half of the case are between 50-69 years of age (n=19, 48%). However, female cases tend to be younger (Mean Age= 54 years) than male cases (Mean Age=62 years).

If you have patients who you feel may meet the case definition for this novel neurological syndrome, please send a clinical referral to Dr. Alier Marrero at the Mind Clinic
Fax: (506) 870 2841
Phone: (506) 8575569

If you have patients who you feel may meet the case definition for CJD, please report by following routine reporting process for Creutzfeld-Jacob disease. These cases will be referred back to the Mind Clinic if they are subsequently found to fit this New Brunswick cluster.

Thank you for your continued collaboration.

Dans l'ensemble, les cas sont répartis de manière égale entre les hommes (n=20, 50 %) et les femmes (n=20, 50 %). L'âge médian est de 59 ans. Environ la moitié des cas ont entre 50 et 69 ans (n=19, 48 %). Toutefois, les cas féminins ont tendance à être plus jeunes (âge moyen = 54 ans) que les cas masculins (âge moyen = 62 ans).

Si vous avez des patients qui, à votre avis, peuvent correspondre à la définition de cas pour ce nouveau syndrome neurologique, veuillez envoyer une référence vers les soins cliniques au Dr Alier Marrero à la Mind Clinic :
Fax: (506) 870 2841
Phone: (506) 8575569

Si vous avez des patients qui, à votre avis, peuvent correspondre à la définition de MCJ, veuillez les signaler en suivant la procédure de déclaration de routine pour la maladie de Creutzfeldt-Jacob. Ces cas seront aiguillés à nouveau vers la Mind Clinic s'ils se révèlent correspondre à cette grappe de cas au Nouveau-Brunswick.

Nous vous remercions de votre collaboration continue.



Dr. / D^{re} Cristin Muecke, MD, MSc, FRCPC
Deputy Chief Medical Officer of Health / Médecin-hygiéniste en chef adjointe

Appendix 1: Case Definition

(Elaborated by Dr. Alier Marrero, Dr. Michael Coulthart, Dr. Gerard Jansen and the National Surveillance System for Creutzfeldt-Jakob Disease)

**Case Definition (draft as of Jan 29, 2021)
Progressive Neurological Syndrome of Unknown Etiology
Among Adults in New Brunswick, Canada**

Confirmed Case:

Progressive neurological syndrome involving rapidly progressing dementia and at least four of the following clinical features, verified directly where possible by a physician:

- Cerebellar ataxia (gait ataxia, truncal ataxia, cerebellar dysarthria or dysmetria), abnormal cerebellar function test or cerebellar symptoms (dysdiadochokinesis, intention tremor etc.)
- Psychiatric symptoms (agitation/irritability, aggressiveness, apathy/withdrawal, anxiety or obsessive behaviour)
- Visual hallucinations, cortical blindness or other cortical visual symptoms
- Pyramidal or extrapyramidal signs, including atypical Parkinsonism
- Myoclonus
- Painful sensory symptoms (limb pain, dysesthesia or paresthesia) persisting for six months or more, in absence of peripheral nervous system dysfunction
- Muscle atrophy

The majority of these should manifest during the first 18-36 months of illness

AND

One or more of the following findings from supporting investigations:

- Atrophy, greater than expected for age on MRI
- EEG slowing or hypoperfusion on SPECT (CT) or hypometabolism on PET-CT scan

AND

Insufficient evidence for an alternative diagnosis, including known forms of human prion disease

Suspect Case:

Progressive neurological syndrome involving at least four of the following clinical features, verified directly where possible by a health care provider:

- Rapidly progressing dementia
- Cerebellar ataxia (gait ataxia, truncal ataxia, cerebellar dysarthria or dysmetria), abnormal cerebellar function test or cerebellar symptoms (dysdiadochokinesis, intention tremor etc.)
- Psychiatric symptoms (agitation/irritability, aggressiveness, apathy/withdrawal, anxiety or obsessive behaviour)
- Visual hallucinations, cortical blindness or other cortical visual symptoms
- Pyramidal or extrapyramidal signs, including atypical Parkinsonism
- Myoclonus
- Painful sensory symptoms (limb pain, dysesthesia or paresthesia) persisting for six months or more, in absence of peripheral nervous system dysfunction
- Muscle atrophy

The majority of these should manifest during the first 18-36 months of illness.

AND

Insufficient evidence for an alternative diagnosis.

Appendix C – October 26, 2021 Memo



Memo Note

Department of Health / Ministère de la Santé
Office of the Chief Medical Officer of Health /
Bureau du médecin-hygiéniste en chef
P.O. Box/C.P. 5100
Fredericton, NB E3B 5G8
Tel/Tél. (506) 457-4800
Fax/Télé. (506) 453-2780

Date : October 26, 2021 / Le 26 Octobre 2021

To/Dest. : Health care professionals, NBMS, NANB, NBPA, College of Pharmacists, LPN Association, RHAs (PH and clinical) / Professionnels de la santé, SMNB, AINB, APNB, Ordre des pharmaciens, Association des infirmières et infirmiers du Nouveau-Brunswick (SP et clinique)

From/Exp. : Dr./Dr Yves A. Léger, Acting Deputy Chief Medical Officer of Health / Médecin-hygiéniste en chef adjoint par intérim

Copies : Dr. / D^{re} Jennifer Russell; RMOHs / MHR; Jennifer Elliott, Éric Levesque, Shelley Landsburg, Hanan Smadi, NBHEOC / COUMSNB, Dr. Susan Brien; Dr. Natalie Banville

Subject/Objet : **REVISED Cluster of Progressive Neurological Syndrome of Unknown Etiology in New Brunswick, Canada /RÉVISÉE Grappe de cas du syndrome neurologique progressif d'étiologie inconnue au Nouveau-Brunswick, Canada**

Public Health New Brunswick is actively investigating 48 cases identified between early 2020 and the end of May, 2021, as being part of a cluster of a potential progressive neurological syndrome of unknown cause in New Brunswick.

These individuals were identified as having a clinical presentation that was similar to that associated with Creutzfeldt-Jakob Disease (CJD) yet noted as having atypical characteristics. These referrals all tested negative for known forms of human prion diseases but did not have other clear causes identified at that time.

An Oversight Committee has been established by the provincial government to review the clinical and investigative work associated with this cluster. The committee consists of two co-

Santé publique Nouveau-Brunswick (SPNB) enquête activement sur 48 cas identifiés entre le début de 2020 et la fin de mai 2021 faisant partie d'une grappe d'un potentiel syndrome neurologique progressif de cause inconnue au Nouveau-Brunswick.

Ces personnes ont une présentation clinique similaire à celle associée à la maladie de Creutzfeldt-Jakob (MCJ), mais pour laquelle on note également des caractéristiques atypiques. Elles ont toutes obtenu des résultats négatifs aux tests de dépistage des formes connues de maladies à prions humaines, mais aucune autre cause précise n'avait été déterminée à ce moment-là.

Le gouvernement provincial a formé un comité de surveillance pour examiner les travaux cliniques et d'enquête associés à cette grappe. Le comité est formé de deux coprésidents, de

chairs, six neurologists and one Medical Officer of Health from Public Health New Brunswick.

The six neurologists will review all the case files of the 48 affected patients, provide second opinions on the identified cases, ensure due diligence, and rule out other potential causes.

If you have a patient who you believe meets the case definition for this identified neurological syndrome of unknown etiology (see Appendix A for case definition), please send a clinical referral directly to the MIND clinic:
Phone: (506) 870-2411
Fax: (506) 870-2841

Referrals will be assessed by specialists working with the MIND Clinic to confirm a clinical diagnosis, conduct further investigation and initiate appropriate treatment. On a go-forward basis, the identification of additional patients as potentially having a progressive neurological syndrome of unknown etiology will require the sign-off of 2 specialty physicians.

Please note this does not replace the normal process for patients who you believe meets the case definition for CJD or other prion diseases. Please report such cases by following the routine reporting process for Creutzfeldt-Jacob Disease as established by the national Creutzfeldt-Jakob Disease Surveillance System (CJDSS), including the required notification to your Regional Public Health Office using the *Notifiable Diseases and Events Notification Form* indicated below (check "Creutzfeldt-Jacob Disease"). If you have the CJDSS case number, please indicate that in the form.

We also wish to remind you that unusual

six neurologues et d'un médecin-hygiéniste de SPNB.

Les six neurologues examineront tous les dossiers des 48 patients concernés, fourniront une contre-expertise des cas signalés, assureront une diligence appropriée et écarteront toute autre cause possible.

Si vous avez un patient qui, selon vous, répond à la définition de cas pour ce syndrome neurologique d'étiologie inconnue (voir l'annexe A pour la définition de cas), veuillez envoyer un aiguillage clinique à la MIND Clinic :
Téléphone : 506-870-2411
Télécopieur : 506-870-2841

Les signalements seront évalués par des spécialistes qui travaillent avec la MIND Clinic pour confirmer un diagnostic clinique, faire une enquête plus approfondie et instaurer un traitement approprié. Dorénavant, l'identification des patients supplémentaires comme étant potentiellement atteints d'un syndrome neurologique progressif d'étiologie inconnue nécessitera l'approbation de deux médecins spécialistes.

Veuillez prendre note que cela ne remplace pas le processus normal pour les patients qui, selon vous, répondent à la définition de cas de la MCJ ou d'autres maladies à prions. Veuillez signaler ces cas en suivant la procédure de déclaration de routine pour la MCJ établie dans le cadre du Système de surveillance de la maladie de Creutzfeldt-Jakob (SSMCJ) national, y compris la nécessité d'aviser votre bureau régional de Santé publique au moyen du *Formulaire de signalement des maladies et des événements à déclaration obligatoire* mentionné ci-dessous (cochez « Maladie de Creutzfeldt-Jakob »). Si vous avez le numéro de cas du SSMCJ, veuillez l'indiquer dans le formulaire.

Nous vous rappelons également que les

illnesses are identified as notifiable diseases or events under the Reporting and Diseases Regulation of the Public Health Act. As such, you are required to notify Public Health New Brunswick if you have identified these types of illnesses, using the Notifiable Diseases and Events Notification Form (check “unusual illness”). The form can be found at the following site:

https://www2.gnb.ca/content/gnb/en/departments/ocmoh/for_healthprofessionals/cdc.html

All notifications provided to national entities that involve notifiable diseases or events under the Reporting and Diseases Regulation of the Public Health Act must also be reported to your regional Public Health office.

Thank you for your continued collaboration.

maladies inhabituelles font partie des maladies ou événements à déclaration obligatoire en vertu du *Règlement sur certaines maladies et le protocole de signalement* de la *Loi sur la santé publique*. Par conséquent, vous devez aviser SPNB si vous avez déterminé ces types de maladies au moyen du *Formulaire de signalement des maladies et des événements à déclaration obligatoire* (cochez « Maladie inhabituelle »). Le formulaire est accessible sur le site suivant :

https://www2.gnb.ca/content/gnb/fr/ministeres/bmhc/professionnels_sante/maladie.html

Toutes déclarations fournies aux entités nationales qui concernent des maladies ou des événements à déclaration obligatoire en vertu du *Règlement sur certaines maladies et le protocole de signalement* de la *Loi sur la santé publique* doivent être également signalées à votre bureau régional de Santé publique.

Merci de votre collaboration soutenue.



Dr./Dr Yves A. Léger, MD, MHSc, FRCPC
Acting Deputy Chief Medical Officer of Health / Médecin-hygiéniste en chef adjoint par intérim

Appendix 1: Case Definition

Appendix D – Timeline

