National Lyme Disease Meeting
March 8-9, 2006

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EXECUTIVE SUMMARY

In Canada, diseases transmissible between animals and humans, or zoonotic diseases, represent an increasingly important public health threat and are caused by a wide-range of pathogens including bacterial, viral, fungal, rickettsial, chlamydial, prion and parasitic agents. Zoonotic diseases infect farmed, companion and wild animals as well as humans, and include many agents that are recognized as emerging threats. Lyme disease is a tick transmitted zoonotic disease of bacterial etiology which is currently of growing concern in Canada.

There are many factors, including environmental and climatic changes, changes in human behaviour and travel, urbanization, ecological changes and others, that affect the level of risk associated with zoonotic and vector-borne diseases such as Lyme disease. The documentation of newly identified populations of blacklegged ticks infected with *Borrelia burgdorferi*, the bacteria which causes Lyme disease, in some areas of Manitoba, Ontario and Nova Scotia indicates the need for a broader, systematic approach to tick and human case surveillance, in order to better assess the risk of human infection. Improved understanding of risk would be a driver to developing new approaches in the control, prevention and investigation of Lyme disease in Canada.

On March 8-9th, 2006, the Public Health Agency of Canada sponsored a meeting of national and international scientific experts on Lyme disease, communication experts, provincial representatives, representatives from the Canadian Lyme Disease Foundation and the National ME/FM Action Network. The intent of the meeting was to begin a process to review and update the guidelines from the 1991 consensus conference on Lyme disease. To facilitate this process the meeting reviewed current knowledge on the epidemiology and diagnosis of Lyme disease, and took the opportunity to identify and prioritise research requirements. Consideration was also given to new approaches to surveillance and risk communication of Lyme disease in Canada. The discussion groups, plenary presentations and question and answer periods provided an opportunity to review current guidelines on the epidemiology, diagnosis and treatment of Lyme disease which are based on recommendations from the January 15-16, 1991 Consensus Conference on Lyme disease.

The two-day meeting included presentations which addressed epidemiological, ecological, diagnostic, public health, communications and ethics perspectives and identified significant research findings and issues relating to Lyme disease in Canada and the United States. The plenary sessions provided updates and current information on the epizootiology, diagnosis and laboratory testing, human epidemiology and surveillance, and information and communication of Lyme disease issues.

The tick vector of *B. burgdorferi* in eastern and central Canada, *Ixodes scapularis*, has steadily expanded its range in the United States over the last 30 years, and similar range expansions have been observed in parts of southern Manitoba, eastern Ontario, and Nova Scotia in recent years. The need for systematic sampling for ticks together with ecological risk modelling was identified as key to developing predictive risk maps.

The role of migrating passerine birds in transporting vector ticks (*I. pacificus* and *I. scapularis*) was demonstrated to be one important mechanism for range expansion, and could help to explain the occurrence of human Lyme disease cases in parts of Canada where the vector ticks are not known to be established. The major bird migration routes transect Lyme disease endemic areas of the United States and Canada. Spring migrating birds stop-over to feed at times that coincide

with the seasonal activity of immature stages of *I. pacificus* and *I. scapularis*. This has potential to impact the future range of ticks as well as areas of risk of human infection in Canada. Ongoing expansion of Lyme disease in Canada, however, will be dependent on numerous factors including climate, available habitat, and distribution of potential host species. Current modelling suggests that increased ambient temperatures with climate change could result in expansion of tick range to encompass most of the heavily populated regions of southeastern Canada.

Currently, Lyme disease testing in Canadian Laboratories is based on a two-tiered approach, utilizing an ELISA as a front-line test. Reactors are further examined using IgG and, or IgM western blot tests. This approach is the same as that adopted by the US CDC as the most likely to give the best combination of sensitivity and specificity. However, it was clear in discussions that there were concerns that current testing procedures could miss some patients with Lyme disease. It was acknowledged by all that issues such as the testing approach, stage of disease, the time between tick bite and test, persistence of antibody responses, interpretation of western blot tests, impact of early treatment, and the technical demands of the western blot test can affect test outcomes and that newer and developing test procedures should be evaluated.

While early stage Lyme disease may be characterized by erythma migrans (EM), which is sufficiently distinctive to permit clinical diagnosis by an experienced clinician, acute disseminated disease is characterized by a number of systemic presentations affecting multiple organ systems. Late infection appears to be more specifically associated with neurologic disease and arthritis.

Concern was expressed about suggested links between Lyme disease and Multiple Sclerosis, Chronic Fatigue Syndrome and Fibromyalgia, and the existence of post Lyme disease syndrome, described by some as chronic Lyme disease. Differences were apparent in attendees concerning the existence and definition of what is described as chronic Lyme disease. Part of the problem is the variety of non-specific symptoms associated with the latter, and it was suggested that while it is difficult to relate these symptoms to Lyme disease, the possibility should be further explored.

The number of reported cases of Lyme disease in Canada is relatively low (20-60 new cases reported annually), with over half associated with travel outside of the country. The actual number of cases is undoubtedly higher given that not all clinical cases are captured by current surveillance approaches and there are indications that the incidence of the disease may be increasing. The recent inclusion of Lyme disease as a nationally notifiable disease may help address these issues over time. The use of definitions specifically for surveillance may also help improve ascertainment of case numbers in Canada.

The breakout sessions, which covered the areas of epizootiology, laboratory diagnosis, and human surveillance, provided an opportunity for more in-depth discussions which, in turn, provided recommendations for the revision of the 1991 guidelines and the 1999 national notifiable disease case definition for Lyme disease. Specific comments and recommendations are outlined in the report and will be used as a starting point for revision of the 1991 guidelines.

Discussions in the breakout groups reached consensus on a series of recommendations related to the epizootiology of vector ticks, the definitions (criteria) of tick status in a geographic area, and current distribution of vector ticks in Canada, including the potential role of bird-borne ticks in the future range expansion of tick populations. Consensus was not reached on a number of issues or statements related to the clinical and laboratory diagnosis of Lyme disease due either to disagreement between discussants or because some of the issues identified for discussion were not covered due to lack of time. Some areas of concern could be addressed through clear

communication and understanding of the different objectives of a surveillance case definition versus a clinical case definition, as well as improved description of clinical presentations of Lyme disease. There was consensus in plenary session about the need to establish technical working groups to specifically address the more complex and contentious issues by thorough appraisal of available scientific literature.

Positive steps were taken to recommend changes to the wording of the existing (1991) guidelines to update statements related to evidence of infection, and the use of specific diagnostic tests. In particular, it was re-emphasised that lack of evidence of a visit to an area where Lyme disease is established should not influence a clinical consideration of Lyme disease diagnosis in individual patients. Recommendations from the conference should be fully considered in future revisions of a case definition relevant to EM in an individual in a risk area and EM in an individual not in a risk area.

The final plenary session was a discussion on the compiled research needs identified throughout the two days of deliberations and included recommendations covering three key areas: the organism, *B. burgdorferi*, which causes Lyme disease; the disease itself; and the epidemiology of vector ticks. The genetic diversity and pathogenesis of *B. burgdorferi* were identified as current priorities for research. Focus on the disease itself should include improvement in diagnostic technologies and approaches, improvement in understanding the clinical presentations and the burden of disease; and improvement in physician awareness of, and knowledge about, Lyme disease.

There was also consensus among participants on critical key issues and recommended next steps which included the following:

- Establish a group that could craft a set of case definitions, taking into account the need for two sets of definitions, one for surveillance and one for clinical diagnostic purposes.
- Examine the possibility of engaging CIHR in addressing Lyme disease research priorities. This will help in framing more specific questions on research topics identified in this report.
- Identify a mechanism for regular review of the Lyme disease situation and national guidelines.
- Examine approaches for enhancing communications to the public, physicians and public health professionals on Lyme disease risks, prevention and related issues.
- Identify and explore new sources of funding, for example, risk identification and prevention for the 2010 Olympic Games.

Lyme disease poses unique challenges in a changing environment in which further expansion of tick-infested areas and increased risk of human infection are likely to occur. In light of these challenges, the Public Health Agency of Canada will continue to work collaboratively to monitor these risks, enhance diagnostic approaches and provide public health advice, including revision of the 1991 guidelines, based on the best available scientific evidence. Until new guidelines have been approved through the Public Health Network Council, the information in this report may be useful to public health officers and healthcare professionals for consideration in diagnosing, confirming, and reporting cases of Lyme disease in Canada.

INTRODUCTION TO THE REPORT

The Public Health Agency of Canada brought together scientific experts, external stakeholders and other affected jurisdictions to present their own or their organizational perspectives on areas that need to be considered in the control, prevention, and management of Lyme disease in Canada. The report is a compilation of these perspectives and recommendations and unless otherwise stated does not necessarily represent a consensus of all participants.

This report has been divided into two main sections. The first consolidates all plenary presentations and includes the text of the brief Questions and Answers which followed each plenary session. Section two represents the summaries of the breakout groups, each of which presented comments based on specific tasks or questions and included recommendations and discussions on next steps or revisions to the text of the existing guidelines. The report concludes with a brief presentation of next steps and a summary of the proceedings.

The planning committee for the meeting recognized that addressing Lyme disease epidemiology and diagnosis would raise many issues which would challenge the existing guidelines as well as the views of experts and advocacy groups. To help the decision-making process, the committee requested the facilitator to present a decision-making framework to be agreed at the commencement of the meeting. The framework agreed upon at the meeting was based on definitions of different levels of decisions and is outlined below:

- Consensus Decision meant no one has a major objection; everyone can live with it
- Majority Decision means at least 2/3 of participants agree and minority concerns are identified
- Unresolved Issue means there is no consensus or majority decision
- Decisions may include proposals for processes (eg. Expert group) and/or data or research gaps.

WELCOME AND OPENING REMARKS

Introductory Remarks (Paul Sockett)

Paul Sockett, Director, Foodborne, Waterborne and Zoonotic Infections Division, Centre for Infectious Disease Prevention and Control (CIDPC), Public Health Agency of Canada (PHAC), welcomed attendees and guest speakers to the meeting. Dr. Sockett passed on the regrets of the Chief Public Health Officer who was unable to attend the meeting, and offered an invitation, on behalf of the Deputy Chief Public Health Officer, to stakeholder groups to meet with him in the near future to discuss issues and concerns.

Both nationally and internationally, emerging zoonotic diseases are increasingly being recognized as causing increasing risk to public health. Within recent years, notable examples in Canada include Hantavirus, raccoon and bat rabies, West Nile Virus, Tularemia, Lyme disease and Avian Influenza. The Public Health Agency of Canada takes these threats seriously and has directed resources towards addressing these issues.

Lyme disease is of interest and priority to the Public Health Agency of Canada and the Agency is committed to continue working with stakeholders to successfully manage the risk to Canadians. Specifically this will include updating and revising the 1991 *Canadian Lyme disease Guidelines.* Cumulative research and epidemologic studies indicate that the ecology of Lyme disease in Canada is changing and the relevant tick vectors currently have a wider distribution than had been identified in 1991. The number of areas classified under the 1991 guidelines as endemic, has increased from one to seven and the role of various bird species in distributing ticks to non-endemic areas, where people may be exposed, is under investigation. Also, the role of ticks in transmission of diseases such as human granulocytic ehrlichiosis and bartonella needs to be assessed. The dynamic situation makes review and revision of the 1991 guidelines timely and it is hoped that revision of the guidelines will be useful in the diagnosis and control of this potentially debilitating illness.

The general nature and epizootiology of Lyme disease make it necessary to take a comprehensive approach to research, surveillance, diagnostic technology and tick ecology. This will require cooperation and collaboration among many disciplines, jurisdictions and stakeholders.

The objectives of this meeting are to:

- review and revise, as appropriate, the existing 1991 guidelines;
- identify key gaps and needs, particularly in the areas of epizootiology, clinical and laboratory diagnosis, human disease surveillance and communications (treatment is not being covered at this meeting);
- identify and prioritize key areas for research.

To achieve these objectives, the approach will be to review science-based information, to develop recommendations for changes to the 1991 guidelines, to provide a rationale for changes to the guidelines, and to make research recommendations.

PLENARY PRESENTATIONS

PLENARY SESSION I: EPIZOOTIOLOGY

Epizootiology of Lyme disease in the United States (Joseph Piesman)

Joseph Piesman, Chief, Tick-Borne Diseases Activity, Centers for Disease Control (CDC), outlined the basic principles of the epizootiology of Lyme disease. The principal tick vectors of Lyme disease spirochetes are *Ixodes scapularis* in eastern North America and *I. pacificus* in western North America. The nymphal stage is the primary vector of the etiologic agent (*Borrelia burgdorferi* sensu strico) to humans. Rodents and birds act as primary reservoirs of the spirochetes, and deer are essential to the cycle, serving as primary hosts for the tick's adult stage, but they are refractory to spirochete infection.

The 1991 Consensus Conference helped lead to the tick mapping project at CDC, which subsequently produced a simple distribution map. The map was very useful at the time, although it had limitations. It did not consider the proportion of ticks infected with the bacteria *B. burgdorferi* or nymphal questing habits, and it was static in time (i.e., not predictive). Even so, it did assist CDC in developing a human risk map for Lyme disease (e.g., where the tick was present, there was considered to be at least a low risk; where the tick was mainly on reptilian hosts instead of small mammals the risk was very low, and where human cases occurred at high incidence there was high to moderate risk). Once a Lyme disease vaccine was available, the tick distribution map and the Lyme disease risk map were used to guide where the vaccine should be used.

Since then, a plethora of studies have extended knowledge and enabled development of model-based risk maps. Although consensus on the best modelling technique is still evolving, experts agree on the need for identifying where ticks are and where they are infecting people. CDC is therefore trying to establish ecological risk modelling on a national scale. Currently, one project (2004–2008) is doing a systematic sampling of the entire eastern United States (east of the 100th meridian) for questing nymphal *I. scapularis* to support a spatial risk model. The eastern United States was divided, for study purposes, into 90–100 quadrants, and one sampling effort was established in each quadrant. The primary types of ticks collected have been *I. scapularis*, *Amblyomma americanum* (primary human-biting tick in the United States, but rare in Canada) and *Dermacentor variabilis* (American dog tick). Data from 2004 and 2005 have confirmed two discrete populations—in the Northeast (Maryland to Maine and moving inland) and Midwest (Michigan, Wisconsin and Minnesota) of questing nymphal *I. scapularis* infected with *B. burgdorferi*. All populations with greater than 10 nymphs were tested for *B. burgdorferi*. It is hoped that a predictive risk map will be ready for "groundtruthing" by 2008 and will be maintained thereafter.

Ixodes scapularis has slowly but steadily expanded its range over the last 30 years (e.g., Hudson River Valley, New York, Western Massachusetts, coastal Maine). Deer are the main hosts driving range expansion on the mainland. The white-footed mouse has often been shown to be an important reservoir of *B. burgdorferi,* although in one study, vaccination of every white-footed mouse in a given area only decreased the infection rate by 16%, indicating that other hosts play key roles. Infection has also been found in squirrels, chipmunks, shrews, skunks and opossums. Birds also play a role.

Less is known about what reservoirs could be responsible for the *B. burgdorferi* infecting *I. pacificus* in the western states. In California, at least, current thinking is that the western grey squirrel may be a key player. Of the three major ticks found in the Northeast and Midwest, *I. scapularis* is a highly competent vector of *B. burgdorferi; A. americanum* is refractory; and *D. variabilis* can become infected with Lyme disease spirochetes, but does not transmit the spirochete. Increasing understanding of vector competence provides new opportunities to exploit the development of prevention tools which can be used by public health to combat the Lyme disease epidemic.

Lyme Borreliosis Risk Assessment: Animal Surveillance (Ian Barker)

Ian Barker, Director, Ontario/Nunavut Region, Canadian Cooperative Wildlife Health Centre, and Professor, Ontario Veterinary College, University of Guelph, outlined the context of surveillance for vectors of *Borrelia burgdorferi* in Canada. These are:

- to establish the presence and geographic distribution of *B. burgdorferi* vectors;
- to ascertain whether ticks represent adventitious or established populations;
- to calculate the size and density of vector populations;
- to ascertain the prevalence of *B. burgdorferi* infection.

This information is used to infer the risk of human exposure based on the intensity of human use of the habitat and the opportunity of exposure to infected ticks. This, in turn, will influence decisions on the implementation of measures to mitigate the risk of human exposure and subsequent infection or disease.

Surveillance strategies include environmental sampling (drag/flag, picking off clothing), animal host sampling (trap the animals, census the ticks) and staging (optimum time and host, epidemiologic interpretation). Host animals trapped include rodents, other small mammals (e.g., skunks), deer and birds which have often been sampled during bird-banding projects. Passive surveillance is used to detect localities that may merit more intensive surveillance. Decisions for active surveillance are based on temporal and spatial clustering of ticks, tick cluster size and appropriate habitat. In areas of active surveillance, testing for *B. burgdorferi* can be done through direct testing of the ticks or indirect testing on animals using serology (to detect antibody), including opportunistic testing of dogs, small mammal sampling and deer sampling, although questions exist about the sensitivity and validity of the tests. Animal serology testing supplements rather than replaces looking for ticks.
Issues include what form, location and intensity of surveillance is appropriate, what testing methods are best and how to establish human risk of exposure and infection. One possible approach would be to establish a two-tiered surveillance program jointly supported by provincial and federal elements. This could include provincially resourced passive surveillance of people and pets (Lyme disease) including collection of ticks from pets.

A second federally supported active surveillance component would comprise a national repository and database for ticks, and other data collected by passive surveillance in the provinces would enable systematic collection and analysis of biological (ticks, agents, serological outcome) and descriptive (locality, date, host, environments, etc…) information. Based on recognition of tick clusters, federally or provincially, supportive active surveillance could be undertaken to determine the presence, extent and intensity of areas of Lyme borreliosis risk.

A further requirement is the need to address occupational health and safety issues, particularly for staff working in the field. These should address not only exposure to *B. burgdorferi*, but also other possible zoonoses such as Hantavirus as well as accident and personal safety.

Surveillance for *Ixodes scapularis* in Canada (Robbin Lindsay)

Robbin Lindsay, Chief of Field Studies, National Microbiology Laboratory, Public Health Agency of Canada, explained that the primary reservoirs for *Borrelia burgdorferi* in endemic localities in Canada are white-footed mice and deer mice, but there is evidence of other potential reservoir hosts, including birds, small mammals such as squirrels, shrews and voles.

The cycle of enzootic transmission involves *B. burgdorferi* circulating among vector larvae and nymphs and reservoir hosts. There is little evidence of vertical transmission. Asynchronous development of immature ticks (nymphs appearing before larvae) and possibly co-feeding (feeding of nymphs and larvae at the same time) assist in transmission. The bacterium appears to overwinter in ticks and possibly in persistently infected reservoir hosts. Also, the strain of *B. burgdorferi* in circulation may influence transmission dynamics, and possibly the spectrum of human illness.

Surveillance in Canada has focused on identifying established populations of *Ixodes* spp. to identify areas of potential human infection, as outlined in Dr. Barker's presentation. For *I. scapularis* surveillance a passive approach was implemented in most provinces from Saskatchewan eastwards, with active surveillance for established tick populations. The central/eastern distribution of *I. scapularis* identified through the surveillance network is wide, with 2,319 ticks collected from January 1990 to December 2003. Interestingly, most submissions were female ticks (96%); in almost every instance these are submitted as individuals from any given location. Submissions with more than one tick are rare (n = 37). Most ticks were taken from dogs (57%) and most adult ticks were collected from April to July and October to November.

Adventitious ticks have been found over a wide geographic area from Manitoba to Newfoundland, supporting the hypothesis that birds play a major role in transporting these ticks. *Borrelia burgdorferi* was detected in about 12% of these introduced ticks, suggesting a low risk of acquiring Lyme disease in non-endemic areas. Other pathogens are also being detected in the ticks, although at lower rates. Established *I. scapularis* populations have spread significantly since 1991, when only a single location in Ontario was recognised as endemic. Since that time, blacklegged tick populations have been identified at five additional locations including, Point Pelee National Park, Rondeau Provincial Park, the Turkey Point, Long Point in Prince Edward County, Ontario, and in Lunenburg, Nova Scotia. Preliminary evidence of the possible establishment of blacklegged ticks has been obtained at several other localities along Lake Erie and Lake Ontario, although the populations do not appear to have been sustained. Infection rates in host-seeking ticks are quite variable. For example, at Point Pelee, the infection rate is hovering at just about 5%. In Lunenburg, however, the infection rate is about 27% and at Long Point, the infection rates are greater than 50%. In some instances, active surveillance has uncovered potential new foci for Lyme disease and this indicates that distribution is likely to continue to expand, whereas other efforts have failed to identify significant populations. Thus, it is important to refine the active surveillance decision points.

Implementing control measures against ticks in Canada has rarely been undertaken. Part of the reason for this is historically there have been few areas where blacklegged tick populations have become established and these areas have been sparsely populated by humans. Another issue is competing priorities; for example, custodians of some federal or provincial properties such as

parks may see *Ixodes scapularis* as a species deserving of protection, just as species of mammals or birds are protected on parks properties. A bigger hurdle is the availability of acaricides, as few of the broadcast acaricides and none of the products for treatment of animals are registered in Canada. Further, product registration and label modification are industry driven, and the limited Canadian market reduces the incentive for industry to register products here. Fortunately, recent work between the Pest Management Regulatory Agency, public health and industry in dealing with the incursion of West Nile Virus may promote industry engagement. The apparent expansion of blacklegged tick populations into populated areas of Canada necessitates the development and implementation of effective tick control programs, where deemed appropriate.

Thus, to enable future tick control strategies, it is suggested that a multiple-agency working group be established to develop recommendations on the following:

- current options for tick control;
- strengths and weaknesses of each approach;
- anticipated costs and efficacy;
- challenges and hurdles (e.g., product registration);
- other management issues (e.g., engaging industry);
- field studies to develop an efficacy profile in Canada.

Geographic Distribution of *Ixodes scapularis* ticks and *Borrelia burgdorferi* in Canada: Past, Present and Future (Nicholas Ogden)

Nicholas Ogden, a veterinary researcher with the University of Montreal, reviewed the risk of Lyme disease for people in Canada. Because Lyme disease in humans is not transmitted person to person or via food, water or air, but rather by a tick infected with *Borrelia burgdorferi*, the geographic distribution of the disease vector and infective agent is a major predictor of risk. Theoretically, host-seeking ticks are not highly mobile and are tied to particular habitats; in other words, there is minimal disease risk outside endemic regions.

A region is defined as endemic where all three feeding stages of the tick (larva, nymph and adult) are present for two consecutive years, as well as positive laboratory evidence indicating *B. burgdorferi* in ticks or in hosts. Establishing these regions helps to determine where and whether Lyme disease is notifiable and to direct public health awareness and prevention messages, as Lyme disease is largely preventable. Diagnosing Lyme disease clinically and serologically can be difficult; thus, a history of exposure to the endemic region drives diagnostic testing and interpretation of test results.

Studies by John Scott and Mohammed Morshed have indicated that migratory birds are spreading adventitious *Ixodes scapularis* in Canada. Northward-migrating, ground-feeding birds stop over in tick-infested habitats. Spring migration coincides with the spring activity period of *I. scapularis* nymphs, which continuously feed on birds for 5 days (equating to about 500 km of travel during migration) and then drop off into the habitat.

For Lyme disease to more seriously affect Canada, the range of *I. scapularis* would have to expand. Climate, habitat, and the occurrence and abundance of hosts constrain the geographic distribution of reproducing tick populations in Canada at present. The current range of resident, self-sustaining populations is focal but expanding, and the rate of expansion is likely to increase as temperatures rise with climate change. The geographic distribution of bird-borne adventitious

ticks covers most of heavily populated south eastern Canada providing challenges for which surveillance tools are in preparation. However, that said, the definition of "endemic region" needs to be reappraised. Specifically, the risk of Lyme disease should be viewed on a scale rather than simply as present or absent. A high-risk region would be one with reproducing *I. scapularis*; a moderate-risk region would be a zone of range expansion where *I. scapularis* populations are establishing; a low-risk region would have little risk of established tick populations but adventitious ticks are present; and a no-risk region would be beyond the range of migratory bird-borne *I. scapularis*.

Update on the Ecology of Lyme disease and *Ixodes* species on the West Coast (Muhammad Morshed)

Muhammad Morshed, Clinical Microbiologist at the British Columbia Centre for Disease Control (BCCDC), gave an update on Lyme disease in British Columbia, where it was first documented in 1993. Over 21 tick species are documented in British Columbia, with *Ixodes pacificus* and *Dermacentor andersonii* as the two most common types. *I. pacificus* is mostly found in the Lower Mainland, Fraser Valley, and Vancouver Island, and *D. andersonii* in the Interior. From 2000 to 2004, communities (public and physicians) were asked to submit ticks to the BCCDC. Annually, about 400–500 *I. pacificus,* about 50 *Ixodes angustus,* about 200–300 *D. andersonii* and about 20–30 other species were received. All *Ixodes* spp. ticks collected through field studies and received from veterinarians, physicians and the public were cultured for *Borrelia burgdorferi;* of 3,148 tests, 7 (0.22%) were culture positive.

In addition, BCCDC has done active field surveillance (dragging and small animal trapping). Most of the positive ticks found were from the Lower Mainland and Vancouver Island. *Ixodes* spp. have been found as far north as Smithers and as far east as Cranbrook. In 2005, 10 sites were visited for active surveillance, and at a site in Okanagan, *I. angustus* ticks were found as well as one mouse seropositive for Lyme disease.

Genetic analysis of 30 randomly chosen strains from over the years has identified both *B. burgdorferi* sensu stricto and *B. bissettii* present in the province. In addition, ticks have been collected from birds from across Canada to identify the distribution of avian-associated tick species. Several species were found in birds across Canada, including *I. scapularis, I. pacificus, I. brunneus, I. dentatus, I. muris, I. auritulus and Hemophysalis leporispolustris.* Among them *I. scapularis, I pacificus,* and *I. auritulus* were found to carry *B. burgdorferi* spirochetes.

It was noted that the United States uses "established" and "reported" whereas Canada uses "endemic" and "non-endemic" to describe tick populations, and there are different requirements for the presence of larvae, nymphs and adults. Common definitions and terminology would be useful.

Lyme disease and Vector Ticks in Canada (Joan McComas for John Scott)

Joan McComas, Canadian Lyme disease Foundation, presented information on the enzootiology of Lyme disease in Canada on behalf of John D. Scott, Lyme Disease Association of Ontario.

Lyme borreliosis is present in people, domestic animals, and wildlife across Canada. This bacterial zoonosis is caused by the spirochete, *Borrelia burgdorferi* sensu lato (s.l.), and is

transmitted by certain ixodid (hard-bodied) ticks to avian, mammalian, and reptilian hosts. Lyme vector ticks have been documented in all provinces coast to coast. With the exception of Saskatchewan, Lyme disease cases (with no out-of-province travel) and/or *B. burgdorferi* s.l.-infected ticks have been reported in all other provinces. Several established populations of vector ticks are present in localized areas across Canada, and some of these localities are endemic for Lyme disease. Within any given endemic area, *B. burgdorferi* s.l. cycles enzootically between vector ticks and reservoir-competent hosts on a continuous basis.

Borrelia burgdorferi s.l. has many strains and multiple morphological forms. From the cutaneous tick-bite site, spirochetes migrate to all parts of the body causing an aura of clinical manifestations. Some patients may be seronegative and, yet, be very symptomatic. Patients may experience treatment failures and develop persistent, debilitating symptoms. Fatal outcomes have been documented.

Several different *Ixodes* species have been involved in *B. burgdorferi* s.1. transmission in Canada. In central and eastern Canada, the blacklegged tick, *Ixodes scapularis*, acts as the primary vector of Lyme disease. In far-western Canada, the western blacklegged tick, *I. pacificus*, is the principle vector of *B. burgdorferi* s.l. When *I. pacificus* and *I. scapularis* females parasitize hosts (i.e., dogs, cats, horses, and humans), they engorge for approximately 7 days; subadults (larvae, nymphs) normally obtain a blood meal in 2 to 5 days. Transmission of *B. burgdorferi* s.l. commonly takes 36-48 hours; however, when salivary glands are infected, ticks can transmit infection to hosts in a few hours. The attachment of *I. scapularis* adults to mammalian hosts (i.e., dogs, cats, humans) in March and April indicates overwinter survival of this tick species. In southwestern British Columbia, Lyme disease spirochetes have been isolated from subadults of the small mammal tick, *I. angustus*, and parasitized deer mice; this tick species is a potential vector for Lyme disease in humans.

A wide range of terrestrial mammals act as hosts of vector ticks in Canada. The white-footed mouse and the deer mouse, which are both competent reservoirs of *B. burgdorferi* s.l., are prominent hosts of subadult vector ticks. White-tailed deer in eastern and central Canada and mule deer in far-western Canada act as amplifying hosts for the 3 motile development life stages of *I. scapularis* and *I. pacificus*, respectively. In established populations of *I. scapularis* and *I. pacificus*, deer play an important role in helping to sustain tick populations; however, they play a minor role in non-endemic areas. Although *B. burgdorferi* s.1. has been detected in deer, tick-host competency studies with *I. pacificus* and *I. scapularis* ticks have shown that deer lack the substantive attributes of reservoir–competent hosts.

Songbirds disperse ticks that sustain *B. burgdorferi* s.l. and other tick-borne pathogens. These ticks are found mainly on the head and neck of avian hosts. During the spring and summer, *I. pacificus* and *I. scapularis* subadults parasitize ground-foraging passerine birds. For example, the American Robin is a reservoir-competent host of *B. burgdorferi* s.1. After these larval and nymphal ticks are fully engorged, they drop off into tick-friendly habitats. *Ixodes scapularis* subadults have been removed from spring migrants from northern Alberta to Nova Scotia. Likewise, *I. pacificus* have been collected from songbirds in Alberta and British Columbia. Both *I. pacificus* and *I. scapularis* have been detached from spring migrants in Alberta. *Borrelia burgdorferi* s.l.-positive *I. scapularis*, which naturally infests migratory passerines, have been documented in Manitoba, Nova Scotia, and Ontario. Along the Pacific coast, all 3 motile stages of the avian tick, *I. auritulus*, have been collected from songbirds, and some of these ticks harbour *B. burgdorferi* s.l. Although *I. auritulus* is not a human-biting tick, it does play a significant role in the enzootic cycle of the Lyme disease spirochete in some coastal locales.

Our bird-tick studies show that many passerine species transport ticks to Canada during northward spring migration. In North America, migratory passerines travel three main flyways; namely the Altantic, the Mississippi, and the Pacific. These flight paths transect Lyme disease-endemic areas in the northeastern United States, the upper Midwest, and the West Coast, respectively. The main influx of spring migrants make stopovers at these areas to feed and refuel, particularly in May and early June when nymphs of *I. pacificus* and *I. scapularis* peak in their questing activity. Some of these nymphal ticks are infected with *B. burgdorferi* s.l. and other tick-transmitted microorganisms. During spring migration, Neotropical songbirds transport *Amblyomma* species ticks (i.e., the porcupine tick, *A. longirostre*) from as far south as the northern part of South America to central and eastern Canada, a distance spanning 5,000 km or more. Overall, 14 different species of avian-associated ticks have been submitted by bird banders and wildlife rehabilitators Canada-wide. These extended host-parasite relationships provide avenues for long distance and even intercontinental transport of tick-borne diseases.

A 10-year tick-host study in Ontario, conducted by the Lyme Disease Association of Ontario in collaboration with the British Columbia Centre for Disease Control, the University of British Columbia, and Ontario veterinarians, found that *I. scapularis* females are the major vectors of *B. burgdorferi* s.l. for people and pets. Before the attached *I. scapularis* females were tested, the hosts were screened using a tick-host information sheet to make sure that the hosts had no out-of-province travel. Using polymerase chain reaction (PCR) testing, *I. scapularis* females were tested, and a significant percentage were infected with *B. burgdorferi* s.l. Based on our findings, *I. scapularis* adults are the primary vectors of *B. burgdorferi* s.l. for humans and domestic animals in nonendemic areas of central and eastern Canada.

Lyme disease spirochetes cycle enzootically in several established populations of vector ticks across Canada and, from these focal areas, ticks are dispersed randomly by songbirds during resident and migratory flight. People and domestic animals can unknowingly be bitten by ticks while visiting endemic areas or during normal outdoor activities within their own environs; they do not have to go to an endemic area in Canada to contract Lyme disease. Based on the wide dispersal of vector ticks nationwide, and the persistent and debilitating symptoms from late diagnosis and treatment, Canadian physicians must be better educated about Lyme disease.

Discussion and Questions and Answers related to Plenary Session I

Q: Is *Ixodes pacificus* a less competent vector of *Borrelia burgdorferi* or are other factors in play for the lower infection rate than in *Ixodes scapularis*?

A: (Panel Response) *Ixodes pacificus* is a competent vector, but may be less efficient than *Ixodes scapularis.* Also, laboratory tests for *I. pacificus* can be more difficult than for *I. scapularis*, as the nymphs tend not to feed on rodents in the laboratory. Furthermore, climate and feeding habits are at play, as the mammalian population differs in the west and as *I. pacificus* tends to feed on lizards, which are refractory for *Borrelia burgdorferi.*

Q: What is the evidence on *Ixodes angustus* as a high-risk pathogen?

A: (Panel Response) Data from the British Columbia Centre for Disease Control studies over the last 9 years has identified *Ixodes angustus* in various parts of the province, mostly the Interior. In the Squamish (coastal) area, *Borrelia burgdorferi*–positive *I. angustus* have been found, some of

which were taken from humans. An antibody-positive host of *I. angustus* has been found in the Okanagan.

Q: Is there any evidence of Lyme disease vectors and cycles of transmission north of 60°, specifically in the Yukon?

A: (Panel Response) Competent vectors have not currently been documented in the Yukon. It is possible that climate change could eventually enable vector species to exist in the Yukon in the future. Birds migrating to and from the southeast do go to and through the Yukon, but currently that would probably be out of the range for carrying ticks.

PLENARY SESSION II: DIAGNOSIS AND LABORATORY TESTING

Lyme Testing: The New and Old Revisited (Nick Harris)

Nick Harris, President of IGeneX and a Director of the International Lyme and Associated Diseases Society, described the role of the laboratory in the diagnosis of Lyme disease. Testing is conducted because clinical diagnosis of Lyme disease is difficult. Lyme disease symptoms are often confused with multiple sclerosis, chronic fatigue, osteoarthritis, etc... Testing also assures patients that they are receiving the right treatment.

Most laboratory patients do not remember an erythema migrans (EM); however many remember tick-bites throughout their life. If it is a current tick-bite, the emergency room performs an enzyme-linked immunoabsorbent assay (ELISA) at days 2-7. The problem with this approach is that if 'current' refers to 7 days or less after a tick-bite, the test will give a 'false negative'. The second problem is that the ELISA has low sensitivity and specificity. An ideal test should have sensitivity and specificity of greater than or equal to 95%.

The following surveillance case definition was developed for national reporting of Lyme disease by CDC. It was not intended for use in clinical diagnosis:

- **Confirmed Case**: A case with EM, or a case of late manifestation that is laboratory confirmed.
- **Laboratory Confirmation**: Isolation of *Borrelia burgdorferi* from a clinical sample or demonstration of IgM or IgG antibodies to *B. burgdorferi* in serum or CSF. A two-test approach using a sensitive ELISA or IFA, followed by Western blots.

Studies conducted by the group responsible for Lyme disease proficiency testing for the College of American Pathologists (CAP) concluded that the currently available ELISA assays for Lyme disease do not have adequate sensitivity to be part of the two-tiered approach of the CDC/ASHLD, whereby only ELISA-positive samples can be tested by Western blotting.

What should be the standard for Lyme disease diagnosis; the CDC standard or the universal approach? Importantly, Western blots must be read by highly trained individuals. When comparing the frequency of antibody reactivity to various *B. burgdorferi* protein bands among Lyme disease patients, syphilis patients, and normal controls, 41 kDa (kilodaltons) is the most common but not the most specific marker for Lyme disease.

The IgM response to *B. burgdorferi* can be present throughout Lyme disease. Late in the illness, during arthritis, a new IgM response sometimes develops to a 34-kDa component of the

organism. There is further evidence that antibody responses against *B. burgdorferi* can be restricted to IgM even in late Lyme disease of culture positive patients. The persistence of the IgM response can be explained either by a disability to switch antibody production from IgM to IgG or by a continuous appearance of new antigenic epitopes on the spirochetes during the infections. If there is IgG response, it appears in a characteristic sequential pattern over months to years to as many as 21 spirochetal antigens.

It is well documented that antibodies to 31kDa (Osp A) and 34 kDa (Osp B) antigens develop late in Lyme disease or after a re-infection. In late Lyme, these antibodies are often present in tandem. Therefore, it is important to include these two antibodies of importance in the case definition. There is antigenic variation between different strains of *B. burgdorferi*. Thus it is important to use the "correct and multiple strains" for serology and Western blots for optimal sensitivity.

About 20% of Lyme disease patients never make antibodies, and antibodies to *B. burgdorferi*, often are present at only low levels, or are even absent in culture or PCR-positive patients who have been suffering for years from symptoms compatible with Lyme Borreliosis. Therefore, in addition to serological testing, the use of PCR and Lyme antigen detection in diagnosis of Lyme disease is recommended.

It is documented in the literature that the Lyme polymerase chain reaction (PCR) for whole blood and urine give false positive results. On close evaluation of these studies, it was clear that the problem was not the sample type but specificity of the primers used for PCR. We and others have developed PCR tests that are highly specific (> 99%) for all clinical sample types, including urine. The Lyme urine antigen Dot-Blot assay (LDA) detects *B. burgdorferi* antigen in urine. The assay sensitivity is 42% and specificity is 89%, and when confirmed by the reverse Western blot the specificity is greater than 96%.

107 non-vaccinated and non-treated chronic fatigue disease patients' clinical samples, representing 31 families living in an area endemic for Lyme disease were tested. All patients' blood was tested for *B. burgdorferi* antibodies by Western blots (IgG and IgM), and by Lyme Multiplex PCR for *B. burgdorferi* DNA. Urine samples, collected from 105 patients, also were tested for Lyme Multiplex PCR and LDA. If active disease is considered present in patients that are IgM positive, only 32 patients (30%) would have active disease. Since presence of specific DNA or antigen also suggests active disease, PCR added 28 (26%) patients and LDA added 10 (9.5%) patients to the diagnosis (118% increase in sensitivity). Thus, PCR and LDA should be a part of the workup of patients with possible Lyme disease.

In a recent study, 165 sera were tested by Western blots IgG and IgM. All the blots were read by CDC criteria and the 2-band universal criteria. By the 2-band criteria, a sample is considered positive, if any two of the following bands, 23-25, 31, 34, 39, 41 and 83-93 kDa are present on the Western blot. The IgG and IgM Western blot assay specificity by the 2-band criteria was 96% vs. 99% by CDC criteria; however, the overall assay sensitivity improved significantly by the 2-band criteria as compared to the CDC criteria (89% vs. 76%).

Laboratory Testing for Lyme disease (Barbara Johnson)

Barbara Johnson, Chief, Microbiology and Pathogenesis Laboratory, Centers for Disease Control (CDC), described the CDC-advocated two-tiered approach to measuring antibodies: Tier 1 uses an Enzyme-Linked Immunosorbent Assay (ELISA), which is quantitative, and tier 2 uses

immunoblotting, which is qualitative. Lyme disease diagnostics have changed since the CAP surveys in the early 1990s that found the Lyme disease ELISAs insufficiently sensitive. (Some early ELISAs were designed primarily for specificity, which is part of the reason why CDC went with a two-tier approach.) Industry responded to the situation, and about 70 tests have been cleared by the Food and Drug Administration. Many have a high degree of sensitivity.

Is the ELISA sensitive enough to be a first-tier test? It depends on the stage of disease. Whole cell sonicate ELISAs are not useful in the earliest stage of Lyme disease or erythema migrans (EM), and should not be used with these patients. In the later stages of Lyme disease, ELISAs have good sensitivity. Nonetheless, two-tier testing is still essential because the specificity of the ELISA alone is inadequate. Inadequate specificity leads to many false positives (for every 1% drop in specificity, it is estimated that there are 10,000–20,000 false positives). Blotting adds specificity (increasing from about 86% to 98% in one large study), eliminating a huge number of false positives. However, CDC recommends retaining the ELISA as a first step, because Western blots are not quantitative, and because faint bands (especially IgM bands) are often seen in Western blots in samples from healthy donors/or patients with other illnesses.

In Western blot testing, some protein bands are of more diagnostic significance than others. Receiver Operating Characteristic (ROC) analysis (plotting true positives against false positives) indicates that as the number of immunodominant antigens used for testing increases, the specificity increases but the sensitivity decreases. To optimise test performance, the CDC recommendation was set at 2 of 3 bands for IgM blots and 5 bands out of 10 bands for IgG blots.

Seronegative Lyme disease can occur in EM patients, which is why CDC does not recommend testing them. Seronegativity is uncommon in later Lyme disease. In discussing the frequency of seronegative Lyme disease, some people cite studies from the 1980's which were conducted before optimal therapies had been designed and evaluated. There are examples in this literature of people treated inadequately for EM who had their immune response to *Borrelia burgdorferi* aborted and later tested seronegative for Lyme disease. The recent literature ranges widely in conclusions about test sensitivity, which is not surprising since sensitivity varies depending on the proportions of people in the study with early and late disease. It is not helpful to quote aggregated results.

The CDC recommends that IgM testing not be done after about 1 month of illness. Most patients have an IgG response by this time. The predictive value of a positive IgM blot with a negative IgG blot is poor in patients with illness of long duration and when objective clinical signs of Lyme disease are absent.

IgM blots are diagnostically useful in patients with early disseminated Lyme disease (eg. facial palsy, meningitis). At one month after disease onset, some patients may not yet have an IgG response developed fully enough for a blot to be scored positive. Such patients may be retested in about two weeks if the clinical diagnosis remains in doubt. Also, early successful antibiotic therapy can abort immunoglobulin class switch from IgM to IgG, and IgM can persist for a long time.

The CDC does not recommend including OspA and OspB in the criteria for positive Western blots. Although Osp A can be used as a vaccine (antibodies to Osp A mediate killing of borrelia in ticks when they take a blood meal), this fact does not mean that antibodies to Osp A are commonly detected in infected patients. An immune response to these Osps is rarely seen in early disease. In later disease (particularly Lyme arthritis), the immune response has expanded and these patients are almost always seropositive by the recommended blot scoring criteria;

scoring Osp A and Osp B would not add diagnostic value. There is a report in the literature which states that scoring Osp A and Osp B in addition to the currently recommended IgG bands increases sensitivity. This criterion could be considered if validated with samples from other Lyme disease patients and appropriate control samples to document specificity.

In summary, CDC recommends two-tiered testing because the algorithm has high specificity and sensitivity except in early Lyme disease, and experienced laboratories with good quality assurance obtain consistent results. Immunoblotting is useful because the band profiles depend on disease stage and are clinically relevant. Nevertheless, there are limitations. This testing is insensitive for EM patients and it lacks potentially informative antigens that are expressed in mammals but not in cultured organisms. Further, it is complex, technically demanding and costly, and is difficult to standardize. Some laboratories are inexperienced in setting blot cut-off controls. Interpretation requires judgement and experience, and the test is only semi-quantitative. In some settings, patients must have a second blood sample drawn after first tier results are known, and there is a recommendation tied to date of onset of disease, which is not always known with certainty. However, two-tiered testing brought order to the chaotic testing environment that existed in the 1990's, and defines a standard against which to judge new testing approaches. Before new methods of laboratory diagnosis can be recommended, they should be shown to meet, or exceed, the performance characteristics of two-tiered testing by using sound methods of evaluation.

Lyme disease Testing in Canada (Harvey Artsob)

Harvey Artsob, Director, Zoonotic Diseases and Special Pathogens, National Microbiology Laboratory (NML), Public Health Agency of Canada, provided the history of Lyme disease testing in Canada. When human laboratory diagnostic testing for Lyme disease was initiated in the mid-1980s, the NML used its own Enzyme-Linked Immunosorbent Assay (ELISA) and Immunofluorescent Antibody (IFA) tests, which it had developed in house and validated against reference samples obtained from laboratories in the United States and Europe. Although the sensitivity of the ELISA appeared to be excellent, there were serious problems with specificity, with false positives obtained against, for example, syphilis-positive sera. Hence, it was useful only as a front-line screening test. Likewise, the IFA had problems with specificity and is no longer used as a frontline screening test. However, the IFA test is still occasionally used to test ELISA/Western blot–positive sera to demonstrate changes in IgM or IgG titres, as well as in testing animal sera.

In June 1990, a quality control assessment was conducted on Canadian Public Health Laboratories testing for antibodies to *Borrelia burgdorferi*, indicating satisfactory performances with ELISA testing (88.9%–100% sensitivity and reasonable specificity) but a need for upgrading or replacing some IFAs. Three additional quality control assessments were done in 1991, 1992 and 1993, with panels of 27, 10 and 10 sera, respectively. Continuing problems were seen with the IFA test, especially with specificity and with one kit in particular; unfortunately, this test had been used for a published study suggesting (inaccurately) double-digit positivity in some people in Manitoba. There was a subsequent gradual shifting to ELISAs as front-line tests in all Canadian laboratories. Difficulties in obtaining appropriate serum panels and the availability of other proficiency testing networks resulted in the discontinuation of the federal quality assurance program.

Some of the Atlantic provinces send their sera directly to the NML for all testing, and others send them to the Nova Scotia laboratory, which does front-line ELISA testing and sends positives on

to the NML, as do Quebec, Manitoba, Saskatchewan and Alberta. Ontario and British Columbia do their own testing and do not routinely send any sera to the NML.

Six provinces (Quebec, Ontario, Manitoba, Saskatchewan, Alberta and British Columbia) participate in CAP proficiency panels. At the NML, Lyme disease testing consists of two IgM/IgG ELISA tests undertaken simultaneously (only 7 types of Lyme disease tests are licensed in Canada); the NML runs one of the licensed kits in parallel with a C6 ELISA which is an excellent test but is not licensed in Canada; hence the results from the tests are reported as experimental. A matrix IgG Western blot test is undertaken on ELISA reactors. IgM western blots are done only if the date of onset is known to be less than one month or upon special request. Polymerase chain reaction testing is done upon request.

Future steps will include a comparative evaluation of the Lyme disease diagnostic kits currently available in Canada, an attempt to get more tests licensed in Canada (which depends on encouraging industry to apply) and to consider whether more quality assurance initiatives from the NML are necessary.

Discussions and Questions and Answers related to Plenary Session II

Q: To what extent have sera been evaluated for cross-reactivity with non-*burgdorferi* strains?

A: (Panel Response) ELISA tests on human serum samples have shown a high degree of cross-reactivity. Subsequent blot testing improves the specificity but there is still a high rate of false positives.

PLENARY SESSION III:

Clinical Aspects of Lyme disease (Raymond Dattwyler)

Raymond Dattwyler, Professor of Medicine and Microbiology, New York Medical College, discussed Lyme disease clinical manifestations. There are at least 11 species in the *Borrelia* complex, but only *Borrelia burgdorferi* sensu stricto causes North American Lyme disease. Of importance is that Lyme disease is not contagious, ie., there is no human-to-human transmission, rather, it is when *Ixodes* spp. ticks feed on humans that there is transmission. Feeding takes some time, and it is only after about 48 hours of feeding that there is transmission of infection.

The early stage of the disease is characterized by erythema migrans (EM), a skin lesion observed in 80% or more of patients that usually develops 7 to 10 days (range 3–30 days) after the tick bite. Primary EM develops at the site of the tick bite. It is an expanding annular erythematous skin lesion and can grow to be quite large. The lesions are usually painless and nonpruritic. If painful, it is unlikely to be EM. In North America, EM is the only manifestation of Lyme disease that is sufficiently distinctive to allow clinical diagnosis in endemic areas in the absence of laboratory confirmation.

Acute disseminated infection begins with a local infection and spreads to the central nervous system, the heart, other areas of the skin and the joints via the blood stream. It is characterized by meningitis (usually aseptic), cranial neuritis, radiculopathy, arterioventricular block or multiple EM. Cranial neuritis is the most frequent neurologic manifestation of early Lyme disease, with seventh nerve palsy being the most common presentation. In heavily endemic areas, about one in

four patients who present with seventh nerve palsy in spring or late summer have Lyme disease. Lyme meningitis is usually monocytic pleocytosis (< 10% polymorphs), with moderate elevations of cerebral spinal fluid (CSF) protein and normal CSF glucose. Much, however, has changed since the initial descriptions of Lyme disease, which talked about cranial neuritis or meningitis occurring in 15–20% of patients presenting; more recent information indicates that these manifestations may be in 7% or fewer of presenting cases. Similarly, cardiac disease was reported in 7–8% of early cases; more recent reports indicate less than 1%. Tachycardia and palpitations are not symptoms of Lyme disease.

Late infection is characterized by neurologic disease (encephalitis, encephalopathy or peripheral neuropathy) and arthritis. The neurologic disease manifestations are increasingly rare (an informal survey of Lyme disease experts in the United States identified 9 and 7 cases of encephalitis and peripheral neuropathy, respectively, in the past 5 years), probably because of earlier recognition and treatment of Lyme disease. Pathologically, localized inflammatory processes predominate, and there tend to be few constitutional signs or symptoms (e.g., fever, malaise). Despite what some people have thought, neither fatigue nor depression is a common manifestation.

The arthritis of Lyme disease is a monoarticular or oligoarticular large joint arthritis; the knee is the most affected joint. Characteristically the arthritis follows a spontaneous waxing and waning course, with relatively little pain or erythema. It, too, is becoming less frequent (from 24% in early years down to 10% more recently).

Late neurologic Lyme disease is easily differentiated from Multiple Sclerosis (MS). The former is extremely rare, whereas MS is relatively common. Unlike MS, Lyme disease does not follow a relapsing–remitting course and does not cause abnormal evoked responses. Inappropriate diagnosis of Lyme disease in a patient with MS may have serious consequences for the patient resulting in delayed or ineffective treatment.

There is controversy about the frequency and even the existence of post Lyme disease syndrome or chronic Lyme disease. There is no standardized case definition for either of these terms. It is difficult to define syndromes based on such symptoms as fatigue and pain, given the high incidence of fatigue and vague pains without objective signs in the general population.

Issues in the Diagnosis of Lyme disease (Sam Donta)

Sam Donta, Professor of Medicine (Retired), Universities of Iowa and Connecticut, outlined some of the issues in diagnosis throughout the continuum of Lyme disease, from early infection to early disseminated disease and on to late or chronic disease. Generally, the earlier the diagnosis, the earlier the treatment with antibiotics and the better the outcome.

One issue in diagnosing early infection is the high proportion of people who do not notice any tick bite or rash. Furthermore, the erythema migrans (EM) may be typical or atypical. At least one study has shown that up to half of culture-positive rashes are not typical EM. For early disseminated Lyme disease, there are differing opinions about symptomatology. When a patient presents with multiple EM as well as non-specific symptoms (aches, pains, etc.), diagnosis may depend on serology, the issues of which were outlined in earlier presentations at this meeting. With late Lyme disease, the more obvious signs and symptoms (meningitis, seventh nerve palsy, etc.) plus the positive Enzyme-Linked Immunosorbent Assays (ELISA) and more robust Western

blot tests make diagnosis easier. Antibiotics can then be administered and the individuals usually do well.

A major issue area for Lyme disease lies with what is often called post Lyme disease chronic disease. One study identified that 30–50% of people with Lyme disease who were not treated or only partly treated went on to have a variety of constitutional symptoms. Another found that up to 75% of people with Lyme disease have this ill-defined chronic syndrome. Symptoms include fatigue, musculoskeletal problems (e.g., arthralgias), neurocognitive issues (memory problems, concentration difficulties, mood issues) and so-called minor symptoms (headaches, eye symptoms, tremors, sleep dysfunction, etc.). It is very hard to tell whether these symptoms are Lyme disease related, but neither should that possibility be ignored. Interestingly, many of these symptoms coincide with those of the recognized syndromes of chronic fatigue syndrome and fibromyalgia. Both of these syndromes include lists of symptoms, but neither has any identified cause. Dr. Donta suggested that Lyme disease could be one cause of chronic fatigue syndrome.

Finally, Dr. Donta recommended that care be taken in viewing laboratory diagnostics as the ultimate picture. Although people with chronic Lyme disease do not get positive ELISA or Western blot results, which could mean that they do not have Lyme disease, the results could also represent an aberrant response due to a host or *Borrelia* related reaction. Also, if the interpretation of the Western blots was changed to just 1 or 2 significant bands, instead of 5, more positives might be identified. Serologics are not commonly used for infectious disease diagnoses; rather, cultures are the gold standard. Further, some patients who do not show positive on serology respond to Lyme disease treatment. Other diagnostics could also be considered, such as brain spectroscopy. Until better diagnostic tools are developed, it might be pertinent to consider a broader range of clinical symptoms.

PLENARY SESSION IV: HUMAN EPIDEMIOLOGY AND SURVEILLANCE

Surveillance for Lyme Disease in the United States (Paul Mead)

Paul Mead, Chief, Epidemiology, Microbiology and Diagnostics Activity, Centers for Disease Control and Prevention (CDC), explained that States vary in the legal requirements for reporting, in the surveillance methods used and in the investment in public health infrastructure. All states have at least passive surveillance for Lyme disease, but a number also have active surveillance. Data on cases that meet the surveillance case definition are forwarded electronically to CDC, and provisional data are published weekly in the Morbidity and Mortality Weekly Report (MMWR). Final data are published annually in the MMWR, but it can take some time for all States to sign off on the data and thus enable publication.

Because the erythema migrans (EM) part of the case definition is for surveillance, CDC stipulates that the diagnosis must be made by a physician. In addition, it is recommended that laboratory confirmation be done for all people with no known exposure. Exposure is defined as having been in appropriate habitat in a county in which Lyme disease is endemic. An endemic county is one in which at least two confirmed cases have been previously acquired or in which established populations of a known tick vector are infected with *Borrelia burgdorferi*.

Lyme disease was made nationally notifiable in the United States in 1991. Currently around 20,000 cases are reported to CDC each year; about double the number reported in 1991. Incidence data indicate that a growing number of counties are seeing rates of 500 cases/100,000 population per year or more and there is some hint that infections are becoming more common in

neighbouring counties, which fits well with some of the ecological data showing *Ixodes* spp. ticks are moving into new areas.

Distribution by age and sex (1992–2002) indicates that the disease is bimodal, with peaks in children 5–15 years and adults 50–60 years. Lyme disease is more common in males in all age groups. Data from 2004 reporting cases by month of illness onset indicate that most cases are reported from May to August. About 70% of cases reported to CDC for 2001 and 2002 included clinical information. Of these, about three-quarters are EM only and about one-quarter are other manifestations. Carditis and neurological syndromes represent about 1% of reported cases. There appears to be a bias toward reporting more severe illness.

Surveillance limitations are many. States can change their surveillance practices as they see fit and as budgets allow, which can affect the national picture with respect to case distribution and incidence. In endemic areas of the US, males account for the majority of cases and the modal age is 7 to 9 years, whereas in non-endemic areas, females account for the majority of cases and the modal age jumps to about 40 years. This finding suggests that a significant proportion of "cases" in non-endemic areas may in fact be due to other causes. Southern tick-associated rash illness (STARI; associated with the bite of the Lone Star tick) can complicate diagnosis, causing over-reporting of Lyme disease in some areas. Under-reporting is also another issue, as with all notifiable diseases. Estimates of under reporting for Lyme disease range, from three to twelve fold, which is fairly typical of infectious disease reporting in the United States. Despite the limitations of under- and over-reporting, the results are still useful for public health purposes.

For clinicians, patients presenting with unusual manifestations of a disease can be challenging in terms of differential diagnosis and therefore appropriate treatment. Nevertheless, it is the clinician's goal to correctly diagnose and treat such patients. For epidemiologists, the objectives are different. To enable tracking of the disease over time and across locations, they must try to create case definitions that focus on the clearly identifiable cases. A broader definition would capture more of the outlier cases, but it would also capture other diseases, confounding analysis and reducing or eliminating the usefulness of the data. In designing surveillance systems and case definitions, it is critical to recognize that one size does not fit all. Surveillance costs money, there is no single perfect system. Design must be based on specific objectives, and surveillance should provide data for action.

Lyme disease in Canada 1994–2004 (Peter Buck)

Peter Buck, Epidemiologist and Senior Manager, Zoonoses Section, Foodborne, Waterborne and Zoonotic Infections Division, Public Health Agency of Canada, briefly described the reporting of Lyme disease cases in Canada between 1994 and 2004. Data sources included the Canadian Institute for Health Information (CIHI; a hospital morbidity database), Statistics Canada's Morbidity and Mortality Database and cases reported by the provinces to the Public Health Agency's Notifiable Disease Reporting System (NDRS).

Of the 345 cases reported to the NDRS between 1994 and 2004, 193 (56%) were related to travel outside Canada. Data issues include the differences in provincial reporting before Lyme disease became nationally notifiable. Most recorded cases are from Ontario; reporting from Quebec, which also has had many cases is likely incomplete. Incidence in Canada appears to have been increasing over time; however, this finding needs to be interpreted with some caution. Data collected from the CIHI database (1994–2002) identified 67 individuals hospitalized with a discharge diagnosis of Lyme disease; pediatric cases accounted for 32.8%. The median age of

cases was 53 years in adults and 2 years in pediatric cases. Of the adult cases, 60% were female, and of the pediatric cases, 59% were male. Temporally, the peak of cases is in May, but the data are not conclusive. The hospitalized Lyme disease cases peaked in the 5- to 9-year age group, and there was a slight peak in the 35- to 39-year age group.

The numbers from the CIHI database are based on discharge diagnosis and are not necessarily linked to laboratory confirmation. Only those who were hospitalized are captured, which means there will be under-reporting of cases diagnosed and treated in the community. There may be a differing index of suspicion among clinicians in the different geographic regions.

The NDRS data is limited; Lyme disease was only recently (December 2006) endorsed by the Communicable Disease Network Surveillance to be added back onto the NDRS list. Also, Lyme disease was not reportable in all provinces until 2004. The information collected nationally on cases is limited, for example no data on presentation, exposure or risk factors is recorded.

Lyme disease in Ontario 1989–2002 (Linda Vrbova)

Linda Vrbova, Infectious Disease Epidemiologist, Ontario Ministry of Health and Long-Term Care, presented surveillance data on Lyme disease in Ontario, where it became a reportable disease in 1988. The surveillance system is passive and the number of endemic Lyme disease cases has remained fairly constant at about five cases yearly, with no noticeable increase. Identified risk factors are travel to endemic regions both in and outside of Ontario, camping, middle age (40 to 59 years) and female sex (for endemic cases). *Ixodes scapularis* is the principal tick vector.

The Ontario case definition, based on the 1991 consensus conference document, states that no laboratory confirmation is necessary if the history includes travel to an endemic region. Unfortunately, this means that health units are calling the Ministry to ask for definitions of endemic regions, both within Ontario and in other parts of Canada and the world. There is currently no systematic method for redefining endemic regions to enable practitioners to apply the definition properly. Within Ontario, currently recognised endemic regions include Long Point, Rondeau Provincial Park and Turkey Point.

Surveillance in British Columbia (Bonnie Henry)

Bonnie Henry, Physician Epidemiologist, British Columbia Centre for Disease Control (BCCDC), updated the group on Lyme disease in British Columbia. Lyme disease was first recognised in British Columbia in 1991 and made reportable in 1993. The primary vector in the province is *Ixodes pacificus*.

As in Ontario, British Columbia uses a surveillance case definition based on the 1991 consensus conference. Surveillance objectives are to recognise new areas and new cases of disease. Both laboratory-confirmed and clinical erythema migrans (EM) cases are to be reported to the regional Medical Health Officer. Also, as in Ontario, questions have arisen about endemic areas; in British Columbia, the primary risk area is the Lower Mainland.

The BCCDC testing algorithm follows the Centers for Disease Control and Prevention (CDC) and Public Health Agency of Canada recommendations: screening with Enzyme-Linked Immunosorbent Assay (ELISA) and following up with Western blot. The BCCDC also follows

up in detail with the clinicians testing every Enzyme-Linked Immunosorbvent Assay case because of concerns about false positives in a low prevalence area. Some Polymerase Chain Reaction (PCR) work has been done, although it is still investigational.

Two cases have been reported in 2006 and follow-up investigation is ongoing at the time of this meeting. There are 3 to 7 cases yearly, of which only 5 clinical cases have been reported since 1993, indicating under-reporting is an issue. Of all the cases to date, 54% were female, and 46% were male. The average age was 42 years (median age 48 years; range 4 to 66 years); the female mean was 38 years (median age 40 years; range 4 to 66 years), and the male mean was age 46 years (median age 52 years; range 6 to 65 years). Over 40% of cases were travel-related, mostly to European countries with endemic Lyme disease.

The surveillance system is designed to identify risk, which will in turn assist public health messaging to appropriate communities (e.g., hunters). Because there is no specific public health intervention for an individual once they have been infected, the public health focus is on prevention. More data are needed to enable better risk assessment. Also needed is a way to classify risk areas that would help physicians in diagnosing individuals and that would help BCCDC in determining new areas of disease. The BCCDC advocates the registration of permethrin-impregnated clothing for use in Canada.

Human Surveillance of Lyme disease in Manitoba (Greg Hammond)

Greg Hammond, Director of Public Health, Manitoba Health, provided a surveillance update and spoke about Manitoba's attempts to develop an increased understanding of the role of public health to promote ongoing dialogue among Lyme disease stakeholders and to better engage the general public and health professionals in going forward with this issue. Manitoba's concerns relate to the surveillance case definition, changing diagnostic technology, case management, changing Lyme disease epidemiology, competing agendas and priorities, and communications.

There is legal authority to report notifiable diseases under the *Public Health Act*. In January 1999, several communicable diseases, including Lyme disease, were added to Manitoba's list of notifiable diseases. The protocol on new communicable diseases for surveillance was distributed to health care workers and other stakeholders at the time, and numerous physician communications are sent regularly (e.g., seasonal in the spring and early summer). As in other provinces, however, there is under-reporting, in part because of the range of symptoms, in part because some individuals do not go for treatment and in part because the physicians do not always send in reports.

The case definition includes a statement that the definition is for surveillance purposes and is not meant to guide clinical decision-making. As with other provinces, the Manitoba definition complies with the 1991 guidelines. The province has had 8 cases since the disease became reportable: 1 in 1999, 1 in 2001, 1 in 2004 and 5 in 2005. At least 3 of the cases are related to travel to New England.

The aims of public and stakeholder communications are to provide timely, accurate, understandable and useful information, and to develop trust. Mechanisms include a public website that includes monthly surveillance information and other updates, a Health Links toll free line, newspapers, newsletters from the College of Physicians and meetings with regional health authorities.

Lyme disease surveillance is working, but updates are needed (case definition, testing methods and research). There is an intention to do further collaborative studies, with the National Microbiology Laboratories (NML), Public Health Agency of Canada as the lead, on Lyme disease in southeastern Manitoba where some of the new cases have been identified, and increased communication about Lyme disease awareness and the potentially changing epidemiology of the disease in Manitoba.

Prevalence as a Measure of Burden of Disease in the Population (Daniel Cameron)

Daniel Cameron, a practising physician, epidemiologist, and a Board Member of the International Lyme and Associated Diseases Society (ILADS), explained that incidence is the measure of new cases and is useful for studying causal factors and in evaluating prevention programs. Prevalence, on the other hand, is the measure of new and ongoing cases, which is useful as a measure of burden of disease in a population.

In 1985, a few States started reporting Lyme disease; by 2002 almost every State in the country had concerns. The Centers for Disease Control (CDC) publishes an annual map of incidence cases. The number of confirmed cases has risen to over 20,000 per year in the United States, although under-reporting could mean that the true figure is at least 10 times higher and estimated at up to 200,000 per year of cases meeting the CDC criteria. Incidence would be even higher if the case definition were broadened. The case definition did not include neurologic Lyme disease characterized by memory loss, depression, sleep disturbance, difficulty finding words, fatigue, headaches, and irritability. Subjective manifestations including headaches, joint pain, dizziness, myalgias, paresthesias are not included in the CDC definition. The risk of chronic Lyme disease has been estimated to vary from 0.5% to 62%. The lowest prevalence rates (0.5% to 13%) have been reported in studies limited to patients presenting for timely treatment at the time of an erythema migrans (EM) rash. Patients presenting with delayed treatment after the rash is resolved or who never present with a rash would not be eligible for a trial, restricting enrolment to a presenting EM rash.

Treatment delays of one year were reported in a series of Lyme patients with neuropsychiatric presentations despite an average of two previous physician evaluations. Shorter but significant delays averaging 6 weeks were reported in each of three cohorts: 215 consecutively evaluated patients in Westchester County, New York; patients with neurologic presentations; and patients misdiagnosed as cellulitis rather than Lyme Disease.

Actual practice reflects the best description of the “real world”. The higher risk of chronic Lyme disease (34% and 62%) has been reported in studies not restricting enrollment to subjects presenting with an EM rash.

A study by Asch et al retrospectively evaluated 215 consecutive patients treated for Lyme disease in Westchester County. All subjects fulfilled the CDC case definition for Lyme disease, were anti-Borrelia antibody positive and were diagnosed and treated at least one year before our examination. Patients were seen a mean of 3.2 years after initial treatment. Only 82 (32%) were asymptomatic. Clinically active Lyme disease was found in 19 (9%). The remaining 114 (53%) were found to have persistent symptoms of arthralgia, arthritis, cardiac or neurologic involvement with or without fatigue. The authors concluded that “Despite recognition and treatment, Lyme disease is associated with significant infectious and post infectious sequelae.”

Shadick et al conducted a population-based, retrospective cohort study in which patients with a history of Lyme disease who were previously treated with antibiotics were compared with randomly selected controls. The mean duration from disease onset to study evaluation was 6.2 years. The authors found "13 patients (34%; 95% CI, 19% to 49%) had long-term sequelae from Lyme disease (arthritis or recurrent arthralgias [n = 6], neurocognitive impairment [n = 4], and neuropathy or myelopathy [n = 3])." The Lyme disease group had more arthralgias (61% compared with 16%; $P < 0.0001$); distal paresthesias (16% compared with 2%; $P = 0.03$); concentration difficulties (16% compared with 2%; $P = 0.03$); fatigue (26% compared with 9%; $P = 0.04$), poorer global health status scores ($P = 0.04$), more abnormal joints ($P = 0.02$) and more verbal memory deficits ($P = 0.01$) than did the control group. The authors concluded that "our findings suggest that disseminated Lyme disease may be associated with long-term morbidity."

The prevalence can be estimated by summing the incidence and estimate prevalence cases. The estimated number of chronic Lyme disease cases after a 10 year period assuming a 5% risk would reach 83,000. The estimated number of chronic Lyme disease cases after a 10 year period assuming a 34% risk would reach 567,000.

Citing differing conclusions from two evidence based medicine guidelines on Lyme disease as they relate to recognition and treatment of Lyme disease, Dr Cameron suggested that limiting reporting to incidence cases meeting epidemiologic criteria is labour intensive, limited by under-reporting and biased toward acute, confirmed Lyme disease. Incidence reporting underestimates the number of Lyme disease cases. The total burden of illness of Lyme disease could be better assessed by broadening the surveillance definition to include those cases not meeting epidemiologic criteria. Moreover, including prevalence data would be useful in forecasting the need for services and programs and may better reflect determinants of treatment failure and success, as well as providing a better estimate of the burden of disease that may be between 40% and 230% higher than estimates based on incidence only.

A cohort design allows a cost effective method of assessing the prevalence data needed to understand the burden of Lyme disease. The cohort design has been well described by Shadick et al and Asch et al. A cohort design was more cost effective by requiring only one assessment of a patient failing treatment. Each case in a cohort could be validated. The cohort design can be more inclusive by including differing presentations such as neurologic Lyme disease. The cohort could include patients with both timely and delayed presentations to approximate "actual practice."

PLENARY SESSION V: INFORMATION AND COMMUNICATION

Communicating Public Health: A Strategic Risk Communication Approach (Élaine Chatigny)

Élaine Chatigny, Acting Director General of Communications, Public Health Agency of Canada, noted that the traditional approach to communication is a one-way "tell" approach, with the goal of educating, informing, persuading and motivating. It is an approach that produces good results in high trust/low concern environments. But it is an approach that tends to be counterproductive in low trust/high concern situations: when issues are complicated and technical in nature, when the science and facts are unavailable or are controversial, when the "experts" disagree, when multiple individuals and groups with diverse interests and priorities are involved, and when the communications environment is complex. This environment characterizes the situation around

new or emerging diseases (e.g., pandemic influenza, Lyme disease), thus making it vital to create new communication strategies.

Risk communication is a process, and the experts in this consensus meeting have engaged in one of the preliminary steps by coming together to try to ascertain what is known, what is unknown, what is not agreed upon and what is agreed upon. Risk communication is *not* just a risk message: that is part of it, but a part that comes right at the end. Risk communication is an integral component of risk management. One starts by identifying the issue in public health, technical and scientific experts are brought in, but when risk communications are brought in as part of that process, social sciences are also being included. Making and imposing decisions that do not consider the impact on stakeholders and their beliefs and understanding of the issue is risky.

In social science, intuitive understanding of risk is acceptable. Feelings, not just hard facts, are accepted in risk communication. Decisions are still made based on the evidence, but they are not made just on the scientific evidence: they are made based on scientific, legal, environmental and a host of other evidence, including what people believe and perceive. In other words, risk communication is not just about communicating risk (e.g., teaching, selling, telling or hyping benefits or risks). Risk communication can be particularly difficult when dealing with issues of public health and safety, especially when the science is not definitive and the experts do not agree. Definitive statements in those situations can be risky; even more risky is saying nothing, which can lead to a real lack of trust.

The primary goal of risk communication is to enable decision makers and stakeholders to make well-informed decisions that lead to responsible and ethical risk management, with the key element being that stakeholders are part of the process. This dialogue-based process, however, does not mean that the decision-making power is handed over to the stakeholders. The Public Health Agency, for example, is mandated and has the responsibility to make decisions to which it will be held accountable. But everybody is in a better position at the end of the day if the decision is sensitive to stakeholders and recognizes their attitudes and judgements towards the risk issue. Other key components are that the risk communication process is evidence-based and that much effort is put into evaluation of whether objectives are being achieved.

The risk communication process is based on values, uses multiple communication strategies, includes a pre-test of the strategies or messages and requires continuous evaluation and improvement. Lyme disease is one example. Stakeholders include physicians, Lyme disease patients, their families, ministers of health and others. This meeting is an important first step in the dialogue-based communications process.

Ethical Issues in Health Communication (Lorraine Johnson)

Lorraine Johnson, Lyme Disease Association, discussed how informed consent is the backbone of ethical obligations in health care. Personal autonomy is tightly linked to informed consent, which requires that patient choices be free from manipulation or coercion. To be informed, the patient must be provided with the objective information that is relevant to the medical decision.

The failure to provide objective and unbiased health care information violates the right of the individual to make autonomous decisions. Misleading information erodes public confidence in the government, forecloses democratic debate about health care values, suppresses market place autonomy and research, and may empower some stakeholders at the expense of others. When health care issues stir heated public debate, as Lyme disease does, health care communications

create ethical dilemmas. Misleading information can constitute a form of coercion when the distortion provokes fear or anxiety.

Autonomy is the principle most violated by deceptive communications. Individuals should make their own decisions based on unbiased information, and others should refrain from obstructing that process. Distortions, exaggerations and omissions in health care information are forms of paternalism, which is essentially treating the individual as though not capable of making her or his own decisions about personal medical care. One difficult ethical question is when the individual's right to autonomy should give way to a greater public good. Clearly, there are occasions when society should intervene for the public good (e.g., vaccinations, quarantines). This does not appear to the case for Lyme disease.

In other instances, it may be suggested that treatment options should not be offered until the definitive science is understood; however, for the individual, this could mean an unacceptably lengthy wait for treatment. In addition, one of the ways new treatment options are identified is through the creative thinking of front-line physicians. By providing the public with objective health care information, public health officials can respect the autonomy of patients, support democratic decision-making and rebuild the public's trust in science and medicine.

Opportunities for Research Partnerships (Judith Bray)

Judith Bray, Assistant Director, of the Institute of Infection and Immunity (III), of the Canadian Institutes of Health Research (CIHR), noted that the current conference had made it clear that opportunities for Lyme disease research partnerships exist not just between CIHR and the Public Health Agency of Canada (PHAC), but also with the United States equivalents of these agencies and the Lyme disease associations and foundations in both countries.

The CIHR was launched in 2000 to replace the Medical Research Council. At that time the mandate was expanded to include not just biomedical and clinical research but also research on population and public health, health services and health policies. At the same time, a new emphasis was established on strategic research (although discovery research will continue to receive the bulk, 70%, of funding). CIHR has established a new structure for funding research based on 13 virtual institutes and a multi-disciplinary approach. CIHR is currently funding two projects related to Lyme disease and the regular open CIHR competitions are open to investigations in this area.

Currently, CIHR funds over 8,500 researchers in universities, teaching hospitals and research institutes across Canada, with a $699 million budget for 2005/06. Of every dollar that CIHR receives from the federal government, 94 cents goes directly to Canadian health researchers in every province across the country. The strategic research priorities include microbiologically safe food and water, antimicrobial resistance, HIV/AIDS and hepatitis C, novel vaccine development, emerging infectious diseases, asthma and allergy, organ transplantation and regeneration, autoimmune diseases and innate immunity.

The Institute is keen to work with the Public Health Agency of Canada on the development of programs in overlapping priority areas such as emerging infectious diseases, and in managing the research components of multi-faceted initiatives of common interest. The first step would be to identify the most pressing research questions that might form the foundations of a strategic research initiative focussed on issues related to Lyme disease and other emerging infections, particularly those related to global climate change.

Discussions and Questions and Answers related to Plenary Session V

Q: How is CIHR promoting the interface between ecological or field-based studies and emerging infectious diseases?

A: As mentioned, CIHR is already funding some field-based studies through the open grants competition and the CIHR Institutes are able to create and launch their own strategic research initiative and RFAs, and establish specific grant review panels. In addition, CIHR has formed an ongoing partnership with the Natural Sciences and Engineering Research Council (NSERC) through the Collaborative Health Research Program. This program is designed to bridge the gap between the CIHR and NSERC mandates by providing funding for projects that bring together researchers from the physical, environmental, and life sciences.

BREAKOUT SESSION REPORTS

BREAKOUT SESSION 1

Participants were divided into three groups, with each focusing on questions specific to given areas of the existing guidelines (epizootiology, clinical issues and laboratory diagnostics), with a goal of identifying where changes are needed. It was recognized that groups were being asked to consider a lot of information in a short time frame, and that strongly held opinions would differ. This session was intended as a first step in the process of giving advice to Public Health Agency of Canada on revising the 1991 guidelines.

The detailed discussions which took place in each breakout group were not recorded and the following text, therefore, reflects the summary reports from each breakout group to a plenary session as presented by the rapporteurs. For clarity, the sections of the 1991 guidelines under review by each breakout group are reproduced in full (*italics)* and are followed by summarized recommendations and comments given by the breakout group. Where there was no consensus on a recommended change of text, this is stated.

Epizootiology Group

Current Issue/Question 1.1: Review the Criteria for defining the status of *Ixodes dammini (Id)* in an area

Current Text:
The status of Id in an area is defined as "established," "adventitious" or "not present" in an area according to the following criteria:

1. *Established (endemic):*
   All three stages—larva, nymph, adult—are present in a locality (a contiguous sampling area) on resident animals or in the environment for at least two consecutive years.

2. *Adventitious:*
   Findings are only sporadic, both temporally and spatially, and usually involve a single stage of the tick.

3. *Not Present:*
   Ticks are not found after the following studies:
   - *a. examination, in one locality, of a minimum of 30 small mammals for immature ticks under magnification or by digestion of skins in potassium hydroxide (KOH), at a time of year when immature stages are expected to be present (usually May to August). This gives a 95% probability of detecting infestation at a prevalence of 5% to 10%.*
   - *b. close examination of the head, neck and forequarters of a large enough sample of deer, per hunting or wildlife area, to give 95% probability of detecting adult ticks at a 5% prevalence (e.g., 45 to 60 deer if the population in the unit ranges from 100 to 10,000 deer), at an appropriate time of year (usually 1 October to 15 December).*
   - *c. sampling of the environment for host-seeking ticks using a one-square metre flannel drag or flag, at the appropriate time of year (usually May to August for immature ticks, 1 October to December for adults). This*

should be done during favourable weather, on at least 3 separate days per locality, for a minimum total of 10 person-hours.

Recommendations and comments:

- Revise *Ixodes dammini* to *Ixodes scapularis* ***(taxonomy change and Ixodes dammini is no longer recognized as a specific species)****;*
- Delete endemic ***(endemic does not apply to ticks, established is a more appropriate term)****;*
- Revise the text "not present" to "not reported" ***(not reported is clearer because it is based on passive surveillance)****;*
- Reconsider descriptors for geographic range of tick occurrence to relate to zones of different levels of Lyme disease (Criteria 3);
- Review the criteria for defining Lyme tick status in an area (i.e. review sample size calculation) (Criteria 3b/a);

Issue/Question 1.2: Epizootiology consensus statement

Current Text:
Lyme disease(LD) is a tick-borne infection caused by B. burgdorferi and transmitted primarily by members of the Ixodes ricinus group of ticks. In North America this group is represented by I. dammini (Id), I. pacificus (Ip) and I. scapularis (Is). Id and Ip are known to occur in Canada. On the basis of current knowledge, the only documented area in Canada with a breeding population of Id is Long Point,Lake Erie, Ontario. There are, however, reports of Id elsewhere in Canada.

Recommendations and comments:

- Paragraph needs to be updated to take into account the changing dynamic of tick occurrence.
- Replace comment on Long Point, Ontario with wording that captures the increase in number of established populations.
- It was suggested that a website be established where current informations on tick distribution could be made available.
- Indicate that number of identified populations are expanding.
- Describe the distribution of tick populations in broader terms only, rather than specific localities.
- Passive surveillance of tick vectors indicates *Is* have been found across Canada east of the Rockies not just at established localities. *Ip* have been found east of the Rockies.
- *Ip* ecology differs from *Is* ecology ***(Ip risk exposure is different from Is risk exposure due to host preference, geographical distribution, infection rate etc)***.
- Human risk from adventitious ticks as well as established populations should be recognised.
- Situation is evolving with local spread from established populations and introduction of ticks over broader geographic areas.
- Factors that may be driving changes in tick distribution include the environment, habitat, human activity and climate change.

Issue/Question 1.3: Methods of detecting *B. burgdorferi* in tick vectors and wildlife reservoirs

Current Text:

1. *In regions where Id is endemic.*
   Attempt to demonstrate B. burgdorferi in ticks by examining up to 100 individual nymph or adult ticks by dark-field or Immunofluorescent antibody staining (IFA) for B. burgdorferi. If spirochetes are recognized, attempt isolation and identification of B. burgdorferi.
   a. *in 100 nymphs or adults (in a minimum of 10 pools of 10 ticks), or*
   b. *in 30 individual small mammals by culture of ears and bladders.*

While serologic studies in animal hosts may assist in raising the index of suspicion for B. burgdorferi endemicity, serology must be interpreted with caution; it must not be used to define an area as endemic or non-endemic for B. burgdorferi.

2. *In regions where Ip is endemic.*
   Demonstrate B. burgdorferi in Ip by dark-field microscopy or IFA as a screening test, saving the positive ticks for culture. Culture surveys of small mammals are not appropriate in areas of Ip endemicity since the prevalence of infection is expected to be very low.

3. *In regions where neither Id nor Ip are endemic.*
   Expert opinion, based on current knowledge, is that it is not reasonable or necessary to search for B. burgdorferi in the environment. The wood tick or American dog tick, Dermacentor variabilis, is not a competent vector for LD. Further research into the role of alternative vectors is desirable.

Recommendations and comments:

- Review the methods for detecting *B. burgdorferi* in tick vectors and wildlife for each of the 3 scenarios described
- Scenarios 1 and 2 should be re-written to take into account new knowledge about the sensitivity of detection and new methodologies
- Scenario 3 should be deleted because it is no longer relevant

Issue/Question 1.4: General recommendations regarding epizootiologic surveillance

Current Text:

1. *The approaches to establishment of the status of Ip, Id and B. burgdorferi endemicity described above (see previous questions 1.1 and 1.3) if negative, are sufficient to conclude with reasonable confidence that the LD cycle is not present in nature in a locality.*

2. *Passive surveillance for Id and Ip on people and wild and domestic animals, and examination of deer for Id and Ip, is encouraged. Field investigations for tick endemicity should be guided by knowledge of biology and ecology of tick vectors, and discovery of Id and Ip, or clusters of human LD cases.*

3. *Epidemiologic surveys for LD tick vectors and wildlife reservoirs should be supported.*

4. *A national reporting system for Id and Ip distribution should be established.*

5. *The definition of endemicity of LD in the human population must be based on findings supporting the presence of B. burgdorferi and an efficient vector in the environment (if possible).*

Recommendations and comments:

- Delete statement 1 because it is no longer relevant.
- Modify statement 2 to include projection for range expansion as a means of guiding field investigations.
- Statement 3 should remain unchanged.
- In response to statement 4 it was recommended that the National West Nile Virus surveillance and reporting approach be used as a template for monitoring Is and Ip distribution.
- Modify statement 5 to consider the likelihood of exposure to an infected tick in evaluating human disease.

Clinical Diagnosis Group

This group did not reach consensus on many of the issues or statements; in part this was because there were fundamental differences of opinion between participants on issues relating to prevalence, manifestations, diagnosis and management of Lyme disease.

Consensus may be achievable if there is a number of different approaches. There has to be a clear communication and understanding of two different case definitions. The public health surveillance case definition may be tight and specific especially when trying to define newly recognized Lyme disease endemic areas. A clinical case definition may be less specific and designed to ensure potential Lyme disease cases are identified for treatment. Medical practitioners and healthcare providers are recommended not to use a surveillance case definition for individual diagnosis which may be better served by a clinical case definition.

Issue/Question 2.1: Review the definitions of erythema migrans (EM) and the late manifestations of LD

Current Text:
Erythema migrans (EM)
An erythematous expanding lesion, at least 5 cm in diameter, with central clearing. The lesion occurs within 30 days of exposure. Annular erythematous lesions occurring within 48 hours of a tick bite may represent hypersensitivity reactions and do not qualify as EM.

Recommendations and comments:

- There should be no requirement for central clearing of the EM lesion
- That EM lesions are not usually painful or itchy should be stated
- There is a need for more detail regarding the actual lesion ***(more detailed description of EM including provision of photographs)***

Current Text*:*
Late Manifestations
These include any of the following, when all other known causes have been ruled out:

a) Musculoskeletal system
Recurrent, brief attacks (lasting weeks or months) of physician-observed large joint swelling in one or a few joints or chronic progressive arthritis preceded by brief attacks. Chronic progressive arthritis NOT preceded by brief attacks, chronic symmetric polyarthritis, arthralgias, myalgias, or fibromyalgia syndromes are NOT accepted as criteria for musculoskeletal involvement.

Recommendations and comments:

- Consensus that the first sentence remains unchanged
- No consensus was reached on modification of the second sentence by adding "arthralgias or myalgias may occur on a persisting or relapsing basis"

Current Text*:*
Nervous system Lymphocytic meningitis, cranial neuritis, facial palsy, radiculoneuropathy, or rarely, encephalomyelitis. Headache, fatigue, paresthesias, or stiff neck are NOT accepted as criteria for neurologic involvement.

Recommendations and comments:

- The current definition should be modified. Consensus was reached on the content of the first sentence, however, no consensus was reached on the wording of the second sentence.

Current Text*:*
Cardiovascular system
Acute onset atrioventricular conduction defects that resolve in days to weeks. Palpitations, bradycardia, bundle branch block or myocarditis are NOT accepted as criteria for cardiovascular involvement.

Recommendation and comments:

- The current definition should be modified. Consensus was reached on the content of the first sentence; however, no consensus was reached on the wording of the second sentence.
- Create a working committee to review evidence and revise case definitions as appropriate (majority recommendation).

Issue/Question 2.2: Clinical manifestations suggestive of LD

Current Text:
Dermatologic
EM may occur 3 to 30 days after a tick bite. EM is an expanding, annular, erythematous skin lesion that is characteristically at least 5 cm in diameter and usually not pruritic or tender. Approximately two -thirds of patients with LD will have EM at some time during the acute phase of their illness. EM should be differentiated from fixed drug eruptions and erythema annular. EM is sufficient for diagnosing LD. True EM lesions less than 2 ½ cm in diameter will increase

in size if observed over 24 to 48 hours. Since EM is an early manifestation of LD, serologic testing may be positive in only 29% of patients. Biopsy of EM lesions is encouraged because it may help confirm the disease when specific stains are used.

Recommendations and comments:

- The texts for this section should be revised as it is no longer current as written
- Refer to Question 2.1

Issue/Question 2.3: Disseminated Disease

This section was not discussed by the reporting group.

Issue/Question 2.4: Indications for specific serologic testing for LD

Current Text:

1. *Serologic testing is indicated in patients with EM, and in patients with signs of disseminated LD who have a history of EM or exposure in an endemic area.*

Recommendations and comments:

- The text for this statement should be revised to indicate serologic testing is not generally indicated in patients with EM (consensus).
- Serologic testing is indicated in patients with signs of disseminated LD (this was an unresolved issue)

Current Text:

2. *Obtaining sequential sera from patients with EM in areas not known to have LD can be of diagnostic value and can help to define the geographic distribution of disease.*

Recommendations and comments:

- The text for this section was not felt to be correct as written and should be revised.

Current Text:

3. *Chronic fatigue and fibromyalgia without objective signs of LD are not considered to be manifestations of LD and should not prompt serologic testing.*

Recommendations and comments:

- This statement is not current as written but no agreement was reached on its modification.

Current Text:

4. *Appropriate quantitative CSF antibody levels may be useful for patients with possible neurologic disease; however, tests for this are currently not available in Canada.*

Recommendations and comments:

- This statement is not current as written but no agreement was reached on modification. ***(The two main issues with the statement were that: in many patients with EM early***

treatment blocks antibody production; and the second was a disagreement around serologic testing and what is considered a "positive" result)

Issue/Question 2.5: Interpretation of positive Lyme serology in patients

Current Text:

1. *Interpretation of serologic tests for LD using currently available methods requires consideration of the signs and symptoms of the patient and whether they have been in an area known to have LD. In non-endemic areas, most positive tests will be falsely positive unless there is a very high clinical suspicion of LD. A positive test will confirm illness in a patient with EM or a history of EM and other typical manifestations of disease.*

Recommendations and comments:

- The statement is not current as written, but no agreement was reached on its modification. In particular, no agreement was reached on how much weight should be given to knowing that the patient has visited an endemic area in making the clinical diagnosis.

Given the lack of consensus in this group, there was significant discussion in plenary about establishing one or two working groups to work on these issues with members to represent both the full spectrum of perspectives and people able to review the science objectively. Prior to establishment of that group, terms of reference would need to be drafted (by Public Health Agency of Canada) and approved by the Chief Medical Officers of Health (recognizing that the work would be in Canada's federal/provincial/territories (F/P/T) environment). At this point in the meeting, consensus was not reached on whether there should be one or two working groups; the question was therefore deferred to day two of this meeting. (This was not discussed further).

Laboratory Diagnosis Group

Issue/Question 3.1: Laboratory evidence of *B. burgdorferi* infection

Current Text:

1. *Any one of the following findings, determined in a laboratory of demonstrated competence, provides laboratory evidence of B. burgdorferi infection:*
    a. Immunospecific staining of the spirochete in tissue or body fluid
    b. significant changes in confirmed antibody response to B. burgdorferi in sequential serum samples
    c. serum positive by enzyme-linked immunosorbents assay (ELISA) serology according to recognized cutoff values and also positive by western blot

Recommendations and Comments:

Amend the current text to take the following into consideration:

- Immunospecific staining is not routinely used
- Add laboratory tests as they become validated
- The following tests are not recommended for routine diagnostic use but under specific circumstances could provide evidence of *B. burgdorferi* infection; these include:
  - isolation/culture,
  - immunospecifc staining of the spirochete in tissue or body fluid

- significant changes in confirmed antibody response to *B. burgdorferi* in sequential serum samples

- Modify introductory statements, second clause to say: "The laboratory criteria for *B.burgdorferi* infection."
- Reorder to make serology (c) the first statement
- Modify (c) to say "serum positive or indeterminate ELISA....
- Significant changes in confirmed antibody response to *B. burgdorferi* (b) to new sub-bullet because not routinely used

Issue/Question 3.2: Recommendations for Standardization and Use of Laboratory Tests for Diagnosis of LD

Current Text:

1. *All laboratories in Canada should use the enzyme-linked immunosorbent assay (ELISA) kits*
   (from commercially available source) for initial testing of both IgG and IgM antibodies to B. burgdorferi.

Recommendations and comments:

- The statement is not current as written, seek the input of the Canadian Public Health Laboratory Network (CPHLN) for modification
- Order a Western blot only if a positive or indeterminate ELISA result occurs, or order a Western blot when a negative ELISA occurs, using clinical judgement. ***(Note: cross reference discussion with statement (6) below).***

Current Text:

2. *Additional diagnostic tests, such as immunofluorescent antibody (IFA) tests may be used as an adjunct to the ELISA.*

Recommendations and comments:

- Delete statement as this is now covered under Issue /Question 3.1

Current Text:

3. *Serologic results should be reported as positive, negative or indeterminate, according to defined laboratory criteria. They should not be reported quantitatively.*

Recommendations and comments

- There was no consensus on the wording of this statement reflecting divided views on quantitative reporting; some believe that it is still useful

Current Text:

4. *Significant changes in confirmed antibody response in sequential serum samples are considered to be diagnostic of recent infection.*

Recommendations and comments:

- Delete statement as this is now covered under Issue /Question 3.1c)

Current Text:

5. *When neuroborrelosis is suspected, routine biochemical and cytologic cerebral spinal fluid (CSF) examination is indicated. Reliable specific antibody testing for CSF is not generally available at present.*

Recommendations and comments:

- Modify statement to indicate that a PCR test and/or a culture may be done

Current Text:

6. *Western blot (WB) should be used to confirm the presence of specific antibodies in sera found positive in the initial ELISA test. Some false positive results may be ruled out by WB. Standards for interpretation of Western blot must be developed.*

Recommendations and comments:

- The statement is generally acceptable. Note that standards for interpretation must be agreed on ***(Note: cross-reference to statement 1 above).***

Issue/Question 3.3 Identify other or new approaches to laboratory diagnosis of LD. Note their relevance to routine laboratory diagnosis and recommend approaches to ensure text validation

- The group did not have time to address this question but "other approaches" such as PCR were referred to in sections 3.1 and 3.2.

Issue/Question 3.4: Interpretation of positive Lyme serology in patients

Current Text:
Interpretation of serologic tests for LD using currently available methods requires consideration of the signs and symptoms of the patient and whether they have been in an area known to have LD. In non-endemic areas, most positive tests will be falsely positive unless there is a very high clinical suspicion of LD. A positive test will confirm illness in a patient with EM or a history of EM and other typical manifestations of disease.

A positive serologic test in an asymptomatic patient is of no diagnostic value. Positive serologic tests in a patient with atypical symptoms do not necessarily imply evidence of disease.

Recommendations and comments:

- Delete the first sentence in the second paragraph. ***(The first part of the statement is not useful, because serology tests will not be done on asymptomatic patients.)***
- Knowledge of areas where infected vector ticks are established is useful but not essential for a clinical diagnosis. It should be recognized that tick populations are establishing and Lyme disease is emerging in new localities.

As with the clinical/surveillance breakout group, above, this group did not reach consensus on a number of questions. In plenary, it was agreed to revisit this group of issues on day 2 of the meeting, however, this did not occur due to time constraints.

BREAKOUT SESSION II

Epidemiology and Surveillance Group

Issue/Question 4.1: What approaches to surveillance (e.g., active surveillance methods) should be taken to improve monitoring of the spread of, or presence of, tick populations in the light of the potential role of birds in transporting ticks, changes in animal/vector ranges, and climate change?

Recommendations and comments:

- Formalize passive surveillance for Lyme disease based on federal/provincial co-operation (consensus).
- Develop an active surveillance program driven by passive surveillance and risk maps and accounting for the difference between *Is* and *Ip* (consensus).
- Develop criteria for appropriate use of active vs passive surveillance (consensus).
- Provide timely feedback to public health community via appropriate means at the provincial and federal levels (consensus) (see bullet 4, section 1.4).

Issue/Question 4.2: Investigation of *B. burgdorferi* sub-species

Is investigation of the *B. burgdorferi* sub-species in Canada (in resident tick populations, wildlife hosts and in incoming adventitious ticks) needed to assist in clinical diagnosis, and in treatment and surveillance studies?

Recommendations and comments:

- It was generally agreed such investigations are needed (consensus).
- Develop specific recommendations on possible studies and identify who may be best positioned to carry out the studies (e.g., academia, provincial public health, federal departments, etc).

Recommendations and comments for possible research studies:

- Investigation of spirochete diversity.
- Investigation of spirochete diversity and its associations with geographical and ecological factors.
- Investigation of spirochete diversity and its associations with clinical syndromes and diagnosis.
- Seek funding from granting agencies (e.g., CIHR).

Clinical and Surveillance Group

Issue/Question 5.1: Probable case definition

Current Text:

Probable case. One of the following:

1. *History of exposure in an endemic area and physician recognition of EM as reported by the patient.*
2. *No history of exposure in an endemic area and both of the following:*
    a. at least one clinically compatible late manifestation;
    b. laboratory evidence of B. burgdorferi infection.

Recommendations and comments:

- The 'Probable Case" definition should be updated; for this discussion, the group focused on surveillance related issues.
- For surveillance purposes the term "probable" should be removed; however, the surveillance definition should not be used to exclude clinical diagnoses.
- There was a recognition that new diagnoses, whether early or late, should be included. Cases should be described as "newly identified" rather than "newly acquired".
- Clinical case definition needs to be reviewed.
- A literature review and/or new research to identify gaps to describe the full spectrum of disease in an evidence-based manner is needed.
- It was suggested that a physician could diagnose erythema migrans based on an examination of the lesion or a photograph of the lesion provided by the patient, however no consensus was reached on this recommendation.

Issue/Question: 5.2: Should serologic testing be applied only to individuals who have travelled to known endemic area and/or have signs and symptoms compatible with LD?

Recommendations and comments:

- Serologic testing may be applied to individuals who have signs and symptoms compatible with Lyme disease (consensus).
- Physicians and the patient/public need to be educated about the appropriate use of, and interpretation of, serologic testing (consensus).
- There were concerns about the positive and negative predictive values of test interpretation and it was proposed that providing definitions would avoid variations in interpretation of results.

Issue/Question 5.3: Should there be separate case definitions for clinical diagnosis and surveillance purposes?

Recommendations and Comments:

- Separate case definitions for clinical diagnostic and surveillance purposes was recommended (consensus).

Human Surveillance Group

Issue/Question 6.1: Data on human cases of LD is currently collated annually in Canada. The data collected is provided voluntarily by provinces and territories and is based on case counts, some of which are based on jurisdictional reportable disease lists. LD has recently been added to the list of nationally notifiable diseases. These provide aggregated totals by age, gender and reporting province (that is, the province where the case was diagnosed).

Current Text:
Epidemiology: Consensus statement
Mandatory reporting of LD is recommended in provinces or territories where there is evidence of endemic foci. Voluntary reporting of cases is encouraged in all other areas.
Human studies

a. Standardized collection of data on individual cases provides valuable epidemiologic information;
b. Surveillance of hospital discharge diagnoses identifies cases of LD that have not been reported;
c. Study of hospital discharge databases (HMRI, Med-Echo) helps to assess trends in the occurrence of hospitalization for LD;
d. Serosurveys are generally believed to be of very limited value.

The group was asked to suggest possible (new) approaches to surveillance to improve understanding of human exposure risk factors and disease burden (e.g., population-based studies).

Recommendations and comments:

- LD is now a nationally reportable communicable disease. Provinces should be reminded of their obligation to report notifiable diseases.
- Delete reference to "endemic foci" in the preamble text beginning: Mandatory reporting...
- Delete the Human Studies sections a to d, as these are not routine surveillance approaches

Issue/Question 6.2: The human case definition was designed for surveillance purposes. A revised national surveillance definition for a confirmed case was introduced in 1999. Should the 1999 definition replace the confirmed case definition in the 1991 guideline (above) with or without modification?

Current Text:
The following are surveillance definitions and are not intended to guide clinical management. Failure to meet a surveillance case definition does not preclude treatment which, instead, should be initiated on the basis of clinical judgement. Since the epidemiology of LD is not fully known, and since laboratory methodology is evolving, the case definitions will require review as experience is gained with the disease.

Confirmed case
One of the following:

1. *Isolation of B. burgdorferi from tissue or body fluid by a laboratory of demonstrated competence.*
2. *History of exposure in an endemic area and either of the following:*
   a. erythema migrans observed by a physician
   b. at least one clinically compatible late manifestation and laboratory evidence of B. burgdorferi infection
3. *No history of exposure in an endemic area and both of the following:*
   a. erythema migrans observed by a physician
   b. laboratory evidence of B. burgdorferi infection

1999 Case Definition for Lyme Disease
Confirmed Case
Erythema migrans (EM)[1] or at least one late manifestation[2] with laboratory

confirmation of infection:

- *isolation of Borrelia burgdorferi from an appropriate clinical specimen*

OR

- *detection of diagnostic immunoglobulin M or immunoglobulin G antibodies to B. burgdorferi in serum or cerebrospinal fluid. A two-test approach is recommended using a sensitive enzyme immunoassay or immunofluorescence antibody test followed by Western blot.*

1. *For purposes of surveillance, EM is defined as a skin lesion that typically begins as a red macule or papule and expands over a period of days to weeks to form a large round lesion, often with partial central clearing. A single primary lesion must reach greater than or equal to 5 cm in size. Secondary lesions also may occur. Annular erythematous lesions occurring within several hours of a tick bite represent hypersensitivity reactions and do not qualify as EM. For most patients, the expanding EM lesion is accompanied by other acute symptoms, particularly fatigue, fever, headache, mildly stiff neck, arthralgia, or myalgia. These symptoms are typically intermittent. The diagnosis of EM must be made by a physician. Laboratory confirmation is recommended for persons with no known exposure.*

2. *Late manifestations include any of the following when an alternative explanation is not found:* ***Musculoskeletal system:*** *Recurrent, brief attacks (weeks or months) of objective joint swelling in one or a few joints, sometimes followed by chronic arthritis in one or a few joints. Manifestations not considered diagnostic criteria include chronic progressive arthritis not preceded by brief attacks, and chronic symmetrical polyarthritis. Additionally, arthralgia, myalgia, or fibromyalgia syndromes alone are not criteria for musculoskeletal involvement.*
   Nervous system: *Any of the following, alone or in combination: lymphocytic meningitis; cranial neuritis, particularly facial palsy (may be bilateral); radiculoneuropathy; or (rarely) encephalomyelitis. Encephalomyelitis must be confirmed by demonstration of antibody production against B. burgdorferi in the CSF, evidenced by a higher titre of antibody in CSF than in serum. Headache, fatigue, paresthesia, or mildly stiff neck alone are not criteria for neurologic involvement.*
   Cardiovascular system: *Acute onset of high-grade (2nd-degree or 3rd-degree) atrioventricular conduction defects that resolve in days to weeks and are sometimes associated with myocarditis. Palpitations, bradycardia, bundle branch block, or myocarditis alone are not criteria for cardiovascular involvement.* ***(From National Surveillance Case Definition)***

Recommendations and comments:

- The text for this section should be replaced by the 1999 “confirmed case” definition with additional modification.
- Retain the text at the beginning of the case definitions.
- Change the word “endemic” to “established” throughout and supplement with “presence of human cases” as an additional characteristic.
- Modify 2b to read: at least one manifestation of acute disseminated LD in place of “clinically compatible late” ***(to distinguish from chronic late)***.
- Consider the use of risk categories, (e.g., low-, medium-, to high-risk areas).

- More information is essential for risk assessment (presence of established infected tick populations and identification/reporting of human cases).
- More specific test factor data on new cases is needed.
- Only confirmed cases are currently reported at the national level; the possibility that other cases (e.g., probable) also be recorded should be considered.
- Physicians should be informed of emerging trends regarding ticks and human cases as part of a public health education strategy.
- The roles of physicians, federal and provincial governments and local health authorities in this and other related reporting systems should be delineated.
- Consider the possibility of developing a national reporting website.
- Definitions of "late manifestation", "early", and "acute disseminated" should be provided.
- Use locally acquired human cases as equivalent to evidence of an established tick population.
- Based on the 1999 definition, the relative values of EM and laboratory information for case definitions should be assessed. For example, if high risk zones, then only need EM, otherwise need laboratory confirmation because 100% confirmation is not possible.
- Need to better define probable (more than 50%) and confirmed ***(because this is very useful for the purpose of public health surveillance)***.

There was lengthy plenary discussion about the case definition. It was agreed that the break out group discussions could be used toward future work on a revised definition and should include the relevance of (1) EM in a risk area and (2) EM not in a risk area. The 1991 version includes this definition. Current maps of endemic and LD risk areas should be made more readily available and updated as new information becomes available.

It was proposed that the Public Health Agency of Canada have a research co-ordination office to help to find grant money and co-ordinate research with the provinces and territories.

Issue/Question: 6.3 **Is there value in obtaining baseline data on human serology in different locations in Canada?**

This area was not covered by the reporting group due to lack of time.

Issue/Question: 6.4: How should the sensitivity and specificity of current and novel laboratory diagnostic techniques be quantified for use in Canada for surveillance studies and clinical diagnosis.

This area was not covered by the reporting group due to lack of time.

PLENARY SESSION VII: NEXT STEPS

NEXT STEPS

A brief discussion led by the facilitator, Mr. Robert Mayne, sought to describe research needs, identified during the meeting discussions. These were consolidated into a list of research priorities presented below. The order of the research needs itself was not prioritized.

Research priorities identified throughout the course of the meeting include the following:

- Investigate the genetic diversity of *B. burgdorferi.*

- Utilize physician billing data and hospital separation data for research into burden of illness studies.
- Explore the issues that exist in understanding chronic Lyme disease and treatment failures.
- Conduct research into geographic areas of risk to map presence of ticks and whether they are infected; influence of habitat and climate on tick distribution.
- Evaluate the confidence of diagnostic testing in these areas of risk.
- Examine impacts of Lyme disease on First Nations communities.
- Examine risk perception, behavioural measures related to Lyme disease.
- Examine physician awareness and attitudes about Lyme disease.
- Investigate and evaluate methods of tick control.
- Examine the relationship between late Lyme disease and other neurologic disease (postmortem, tissue samples, etc.).
- Identify approaches to improve diagnostic testing and alternative diagnostic approaches.
- Examine disease pathogenesis.
- Investigate human risk: incidence based on true areas of exposure.
- Examine risk associated with companion animals, occupation.
- Conduct a review of current literature on manifestation, diagnosis, testing, treatment of Lyme disease.

WRAP-UP (Paul Sockett)

This is the beginning of a process. The Public Health Agency of Canada needs to ensure follow-through on the issues identified as well as on the guidelines. For the guidelines, even after the current round of revisions, regular updating must take place as the ecology of LD continues to evolve. Likewise, we must not lose sight of the fact that this is a partnership approach in collaboration with public health and laboratory colleagues. This report will be taken to the Public Health Network and the Chief Medical Officers of Health, making them aware of what took place at this meeting, the directions discussed and the impact at the various levels.

Conclusions:

The main objective of the meeting was to use science-based information and the broad-based perspective of participants to provide recommendations to meet the longer term objectives of:

- Revising, as appropriate, the existing 1991 guidelines and 1999 national notifiable disease case definition.
- Identifying key gaps and needs, particularly in the areas of epizootiology, clinical and laboratory diagnosis, human disease surveillance, and communications.
- Identifying and prioritizing key areas for research.

In the end, because of the broad based representation and the divergent opinions on this complicated disease, the most notable outcome of the meeting was probably the open and inclusive dialogue that was initiated by the meeting. Furthermore all parties continue to demonstrate a commitment to continue to work together by finding common ground from which to commence the challenging task of developing a more current Lyme disease guideline that will be more useful to health care practitioners, Lyme disease sufferers, and other stakeholders. The steps outlined below will serve as common ground from which all stakeholders can take a first step forward in the prevention, control, and management of Lyme disease in Canada.

- Establish a group that could craft a set of case definitions, taking into account the need for two sets of definitions, one for surveillance and one for clinical diagnostic purposes.
- Examine the possibility of engaging CIHR in addressing Lyme disease research priorities. This will help in framing more specific questions on research topics identified in this report.
- Identify a mechanism for regular review of the Lyme disease situation and national guidelines.
- Examine approaches for enhancing communications to the public, physicians and public health professionals on Lyme disease risk prevention and other issues.
- Identify and explore for new sources of funding, for example, risk identification and prevention for the 2010 Olympic Games.

Glossary of Terms

(BCCDC) British Columbia Centre for Disease Control
(CAP) College of American Pathologists
(CCWHC) Canadian Cooperative Wildlife Health Centre
(CDC) Centers for Disease Control
(CDNS) Communicable Disease Network Surveillance
(CIDPC) Centre for Infectious Disease Prevention and Control
(CIHI) Canadian Institute for Health Information
(CIHR) Canadian Institutes of Health Research
(CLDF) Canadian Lyme Disease Foundation
(CM) Clinical Microbiologist
(CPHLN) Canadian Public Health Laboratory Network
(CPHO) Chief Public Health Officer
(CSF) cerebral spinal fluid
(DCPHO) Deputy Chief Public Health Officer
(ELISA) Enzyme-Linked Immunoabsorbent Assay
(EM) erythema migrans
(FDA) Food and Drug Administration
(F/P/T) Federal/Provincial/Territories
(FWZID) Foodborne, Waterborne and Zoonotic Infections Division
(HIV/AIDS) Human Immunodeficiency Virus / Acquired Immunodeficiency Syndrome
(IFA) Immunofluorescent Antibody
(III) Institute of Infection and Immunity
(IgM) Immunoglobulin M
(IgG) Immunoglobulin G
(ILADS) International Lyme and Associated Diseases Society
(LD) Lyme Disease
(LDA) Lyme Disease Association
(LDA) In presentation by Nick Harris LDA refers to *Lyme urine antigen Dot-Blot assay*
(LDAO) Lyme Disease Association of Ontario
(kDa) Kilodalton
(MMWR) Morbidity and Mortality Weekly Report
(MPL) Microbiology and Pathogenesis Laboratory
(MS) Multiple Sclerosis
(NDRS) Notifiable Disease Reporting System
(NML) National Microbiology Laboratory
(NSERC) Natural Sciences and Engineering Research Council
(OMHLC) Ontario Ministry of Health and Long-Term Care
(OVC) Ontario Veterinary College
(PCR) polymerase chain reaction
(PHA) Public Health Act
(PHAC) Public Health Agency of Canada
(PMRA) Pest Management Regulatory Agency
(ROC) Receiver Operating Characteristic
(STARI) Southern tick-associated rash illness
(U of G) University of Guelph
(U of M) University of Montreal
(Wb) Western blot
(WNV) West Nile virus

(ZDSP) Zoonotic Diseases and Special Pathogens

National Lyme Disease Meeting

March 8 & 9, 2006

Park Plaza Toronto Airport Hotel, Toronto, ON
Algonquin Ballroom – Lower Level

AGENDA

DAY I

Chair: Paul Sockett
Facilitator: Robert Mayne

WELCOME AND OPENING REMARKS

08:15	Introductory Remarks	Paul Sockett
08:30	Welcome and Consensus Building	Paul Sockett and Robert Mayne

PLENARY SESSION I: EPIZOOTIOLOGY

08:45	Epizootiology of Lyme Disease in the United States	Joseph Piesman
09:15	Lyme Borreliosis Risk Assessment: Animal Surveillance	Ian Barker
09:30	Surveillance for *Ixodes scapularis* in Canada	Robbin Lindsay
09:45	Geographic distribution of *Ixodes scapularis* ticks and *Borrelia burgdorferi* in Canada: past, present and future	Nicholas Ogden
10:00	Update on Ecology of Lyme Disease and *Ixodes Species* in the West Coast	Muhammad Morshed
10:15	Lyme Disease and Vector Ticks in Canada	Joan McComas
10:45	*Health Break - Served in the Foyer*	

PLENARY SESSION II: CLINICAL DIAGNOSIS AND LABORATORY DIAGNOSIS

11:00	Lyme Testing: The New and Old Revisited	Nick Harris
11:30	Laboratory Testing for Lyme Disease	Barbara Johnson
12:00	Lyme Disease Testing in Canada	Harvey Artsob

12:20	*Lunch - Served in the Foyer*	
13:20	Clinical Aspects of Lyme Disease	Raymond Dattwyler
13:50	Issues in the Diagnosis of Lyme Disease	Sam Donta

BREAKOUT SESSION I

14:15	Breakout Sessions	
15:00	Health Break	

PLENARY SESSION III: BREAKOUT SESSION I - REPORTS

16:00	Green Breakout Group	Ian Barker
16:20	Red Breakout Group	Bill Bowie
16:40	Blue Breakout Group	Daniel Cameron
17:00	Wrap-up	Paul Sockett
17:10	Adjournment	

National Lyme Disease Meeting

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AGENDA

DAY 2

Chair: Paul Sockett

Facilitator: Robert Mayne

PLENARY SESSION IV: HUMAN EPIDEMIOLOGY AND SURVEILLANCE

08:30	Surveillance for Lyme Disease in the United States	Paul Mead
09:00	Lyme Disease in Canada 1994-2004	Peter Buck

09:10	Lyme Disease in Ontario	Linda Vrbova
09:25	Surveillance for Lyme Disease in British Columbia	Bonnie Henry
09:40	Human Surveillance of Lyme Disease in Manitoba	Greg Hammond
09:55	Prevalence as a Measure of Burden of Disease in the Population	Daniel Cameron
10:20	*Health Break*	

BREAKOUT SESSION II

10:35	Breakout Sessions	
12:00	*Lunch*	

PLENARY SESSION V: BREAKOUT SESSION II - REPORTS

13:00	Green Breakout Group	Ian Barker
13:20	Red Breakout Group	Allison Bested
13:40	Blue Breakout Group	Bonnie Henry

PLENARY SESSION VI: INFORMATION/COMMUNICATION

13:50	Communicating Public Health: A Strategic Risk Communication Approach	Élaine Chatigny
14:20	Ethical Issues in Health Communication	Lorraine Johnson
14:50	Opportunities for a PHAC/CIHR Partnership	Judith Bray
15:10	*Health Break*	
15:25	Open Discussion	

PLENARY SESSION VII: NEXT STEPS

15:50	Next Steps and Priorities	Robert Mayne
16:25	Wrap-up	Paul Sockett
16:30	Adjournment	

List of Participants/ Liste des participants

Park Plaza Toronto Airport Hotel
March 8 & 9, 2006/ le 8 & 9 mars 2006

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