Consensus Conference on Lyme Disease

The Consensus Conference on Lyme Disease was held Jan. 15 and 16, 1991, at the University of Guelph, Guelph, Ont. It was cosponsored by the Laboratory Centre for Disease Control, the Department of National Health and Welfare and the Canadian Society of Infectious Diseases. The purpose of the conference was to achieve a consensus on issues related to Lyme disease and to produce consensus statements in four areas: epizootiology, epidemiology, clinical practice and laboratory investigation.

Participants included representatives from universities and governments across Canada and specialists from the United States (which has a much higher incidence of Lyme disease than Canada) who presented background papers reflecting their experience and expertise in each of the four areas.

Statements emerging from workshop discussions reflect consensus based on current knowledge and are subject to change in the light of ongoing research. These statements are intended to serve as a guide for those involved in the investigation, control and treatment of Lyme disease in Canada.

**EPIZOOTIOLOGY**

Lyme disease is a tick-borne infection caused by *Borrelia 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*. 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, Ont. However, there have been reports of Id elsewhere in Canada.

**Criteria for defining the status of Id in an area**

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

**Established (endemic)**

All three stages — larva, nymph and adult — are present in a locality (a contiguous sampling area) on resident animals or in the environment for at least 2 consecutive years.

**Adventitious**

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

**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 at a time of year when immature stages are expected to be present (usually May to August), which 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

*Adaptations of these approaches appropriate to the biology of Ip should be applied to establish its status in a locality. Further research is necessary to establish appropriate approaches to defining the status of Ip in the Canadian environment.*

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Reprint requests to: Eleanor Paulson, Editor, Canada Diseases Weekly Report, Bureau of Communicable Disease Epidemiology, Laboratory Centre for Disease Control, Tunney's Pasture, Ottawa, ON K1A 0L2
of deer, in a hunting or wildlife area, to give a 95% probability of detecting adult ticks at a prevalence of 5% (e.g., 45 to 60 deer if the population in the unit is 100 to 10 000 deer) at an appropriate time of year (usually Oct. 1 to Dec. 15); (c) sampling of the environment for host-seeking ticks using a 1-m² flannel drag or flag at the appropriate time of year (usually May to August for immature ticks, October to Dec. 1 for adults) during favourable weather, on at least three separate days per locality, for at least 10 person-hours.

On the basis of these definitions the population of ticks at Long Point, Lake Erie, is classified as “established.” All other recorded findings of Id are classified as “adventitious.”

Detection of *B. burgdorferi* in tick vectors and wildlife reservoirs

**Id-endemic regions**

Attempt to demonstrate *B. burgdorferi* in ticks by examining up to 100 nymph or adult ticks by means of darkfield 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 at least 10 pools of 10 ticks) or (b) in 30 small mammals through culture of ears and bladders.

Although serologic studies in animal hosts may assist in raising the index of suspicion for *B. burgdorferi* endemicity, the findings must be interpreted with caution; they must not be used to define an area as endemic or nonendemic for *B. burgdorferi*.

**Ip-endemic regions**

Demonstrate *B. burgdorferi* in Ip by means of darkfield microscopy or IFA as a screening test; save the infected ticks for culture. Culture surveys of small mammals are not appropriate in Ip-endemic areas since the prevalence of infection is expected to be very low.

**Regions not endemic for Id or Ip**

According to expert opinion, based on current knowledge, it is unreasonable and unnecessary to search for *B. burgdorferi* in the environment. The wood tick or American dog tick *Dermacentor variabilis* is not a competent vector for Lyme disease. Further research into the role of other vectors is desirable.

Epizootiotic surveillance

- If the approaches to establishing the status of *Ip, Id and B. burgdorferi* endemicity, as described in the previous section, yield negative results, one can conclude with reasonable confidence that the Lyme disease cycle is not present in nature in that locality.
  - Passive surveillance for Id and Ip among people and wild and domestic animals as well as examination of deer for Id and Ip is encouraged. Field investigations for tick endemicity should be guided by knowledge of the biologic and ecologic characteristics of tick vectors and the discovery of Id and Ip or clusters of Lyme disease in humans.
  - Epidemiologic surveys for tick vectors and wildlife reservoirs should be supported.
  - A national reporting system for Id and Ip distribution should be established.
  - The definition of endemicity of Lyme disease in the human population must be based on findings supporting the presence of *B. burgdorferi* and an efficient vector in the environment (if possible).

**Epidemiology**

Lyme disease is generally rare in Canada, only 140 cases having been reported between 1984 and 1990. Since case definitions were not nationally standardized and often imprecise, many of the reported cases would probably not meet the new surveillance case definitions presented in this section. Most (100 [71%]) of the cases were reported from Ontario. Of the 40 remaining cases 17 were from Manitoba, 11 from British Columbia, 5 each from New Brunswick and Quebec, and 1 each from Newfoundland and Saskatchewan. In all, 42% of the Ontario cases and 98% of those reported from the other provinces had a history of travel to a recognized endemic area outside of the reporting province during the presumed incubation period.

Use of the new case definitions to re-evaluate existing cases and to assess those reported from ongoing surveillance will be instrumental in obtaining a more accurate estimate of the frequency of Lyme disease in Canada. Mandatory reporting is recommended in provinces or territories where there is evidence of endemic foci. Voluntary reporting of cases is encouraged in all other areas.

**Monitoring of trends in low-incidence areas**

The trigger for both human and epizootiologic studies is the occurrence of human cases or vector ticks that may be made known through passive surveillance methods.

**Human studies**

- Standardized collection of data on individual cases provides valuable epidemiologic information.
• Surveillance of hospital discharge diagnoses identifies cases that have not been reported.
• Study of hospital discharge databases (HMRI, Med-Echo) helps to assess trends in hospital admissions because of Lyme disease.
• Serosurveys are generally believed to be of very limited value.

**Epizootiologic studies**

Epizootiologic studies monitor trends in the distribution of Id and other potential vectors.

**Surveillance case definitions**

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

**Confirmed case**

A confirmed case is one in which one of the following is present: (a) isolation of *B. burgdorferi* from tissue or body fluid by a laboratory of demonstrated competence; (b) a history of exposure in an endemic area and either erythema migrans observed by a physician or at least one clinically compatible late manifestation and laboratory evidence of *B. burgdorferi* infection; or (c) no history of exposure in an endemic area but erythema migrans observed by a physician and laboratory evidence of *B. burgdorferi* infection.

**Probable case**

A probable case is one in which one of the following applies: (a) a history of exposure in an endemic area and physician recognition of erythema migrans as reported by the patient; or (b) no history of exposure in an endemic area but at least one clinically compatible late manifestation and laboratory evidence of *B. burgdorferi* infection.

**Exposure in an endemic area**

Exposure such as living in or visiting an endemic area should have occurred no more than 30 days before the onset of erythema migrans or no more than 1 year before the onset of late manifestations. A history of a tick bite is not required.

An endemic area is one in which the risk of transmission of Lyme disease to humans is supported by either (a) the presence of an established vector population known to be infected with *B. burgdorferi* or (b) the occurrence of at least three confirmed human cases, with adequate histories, in which there is no history of exposure in previously identified endemic areas (a provisional definition of an endemic area in the absence of appropriate tick studies).

There is no time limit within which cases must occur or infected vectors must be identified for an area to be declared endemic. The geographic limits of the endemic area will be defined by the provincial or territorial health authorities.

**Erythema migrans**

Erythema migrans is an expanding, annular, erythematous lesion at least 5 cm in diameter with central clearing and is usually not pruritic or tender. The lesion may occur 3 to 30 days after a tick bite. Lesions occurring within 48 hours after a tick bite may represent hypersensitivity reactions and do not qualify as erythema migrans.

**Late manifestations**

These include any of the following, after all other known causes have been ruled out.

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

**Nervous system:** Lymphocytic meningitis, cranial neuritis, facial palsy, radiculoneuropathy and, rarely, encephalomyelitis. Headache, fatigue, paresthesias and stiff neck are not criteria for neurologic involvement.

**Cardiovascular system:** Acute-onset atrioventricular conduction defects that resolve in days to weeks. Palpitations, bradycardia, bundle-branch block and myocarditis are not criteria for cardiovascular involvement.

**Laboratory evidence of *B. burgdorferi* infection**

Any one of the following findings, determined by a laboratory of demonstrated competence, provides evidence of *B. burgdorferi* infection: (a) detec-

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*Developed by the Advisory Committee on Epidemiology in collaboration with the Technical Advisory Committee. For clinical manifestations and guidelines for the treatment of Lyme disease refer to the section on clinical practice.*
tion of the spirochete through immunospecific staining of tissue or body fluid; (b) significant changes in confirmed antibody response to *B. burgdorferi* in sequential serum samples; and (c) positive results of enzyme-linked immunosorbent assay (ELISA) according to recognized cutoff values and positive results of the Western blot technique.

**Case definitions in Canada and the United States**

A Canadian confirmed case would meet the current US confirmed case definition. A US confirmed case would meet either the Canadian confirmed or probable case definition depending on whether there was exposure in an endemic area.

The reasons for differentiating between endemic and nonendemic areas are (a) to obtain more accurate incidence figures for low-incidence areas (most of Canada) by reducing the number of false-positive results among those who meet the case definition; (b) to provide a focus for preventive activities; and (c) to identify areas for epizootiologic study.

The incidence of Lyme disease is so much higher in the United States than in Canada that slight differences in the case definitions are unlikely to affect comparisons of incidence in the two countries.

**Dissemination of accurate information**

In local public health jurisdictions a central person or agency should provide all information to health care workers and the public (including the media). Information should be accurate, be updated frequently and be provided in different formats.

**Health care workers**

The medical community needs information on the diagnosis and management of patients with Lyme disease, including interpretation of laboratory results, treatment guidelines and case reporting. Public health workers need guidelines for investigating and following up reported cases. Veterinarians need information about such factors as the incidence of Lyme disease and the presence of vectors.

These groups can be approached through professional organizations, newsletters and continuing education programs.

**The public**

The public needs accurate information on the incidence of Lyme disease, the presence of vectors, the prevention of tick bites, the signs and symptoms of Lyme disease, the availability of treatment and the prognosis.

Approaches to the public include media releases, fact sheets, brochures, posters and community meetings. Involvement with advocacy groups may be useful if there is a constructive relationship that permits the sharing of resources and information.

**Clinical practice**

Lyme disease is an illness with dermatologic, neurologic, cardiac and rheumatologic signs and symptoms. Patients may present with localized skin involvement (erythema migrans) or disseminated acute or chronic disease. Most patients do not know whether they have been bitten by a tick before the onset of symptoms. Patients who do not meet the surveillance case definitions may be eligible for treatment on the basis of clinical manifestations.

**Clinical manifestations**

**Localized disease**

*Dermatologic involvement*: Approximately two-thirds of patients with Lyme disease will have erythema migrans at some time during the acute phase of the illness. Erythema migrans should be differentiated from fixed drug eruptions and erythema annulare. *The presence of erythema migrans is sufficient for diagnosing Lyme disease.* True lesions less than 2½ cm in diameter will increase in size if observed over 24 to 48 hours. Since erythema migrans is an early manifestation serologic testing may yield positive results in only 20% of patients. Biopsy of the lesions is encouraged because it may help confirm the disease when specific stains are used.

**Disseminated disease**

*Dermatologic involvement*: Multiple erythema migrans lesions indicate disseminated disease, and any associated neurologic symptoms, including headache, should be carefully evaluated.

*Neurologic involvement*: Of patients with Lyme disease 15% to 20% may have neurologic signs and can present with the disseminated acute and chronic forms of the disease. Bell's palsy, lymphocytic meningitis, other cranial or radicular neuropathies or meningoencephalitis may occur but are unlikely to be the only manifestations in nonendemic areas. Cerebrospinal fluid (CSF) should be examined in patients with neurologic signs or symptoms.

*Cardiac involvement*: Cardiac disease occurs in 4% to 8% of patients with Lyme disease. Acute onset of first-degree, second-degree or third-degree atrio-
ventricular conduction defects may occur with the disseminated acute form of the disease, but these conditions are usually transient. Isolated conduction defects are unlikely to be due to Lyme disease in patients who have not been in endemic areas.

**Rheumatologic involvement:** Arthritic involvement is characterized by recurrent, brief attacks (lasting weeks or months) of swelling in one or a few large joints. Uncommonly, chronic progressive (erosive) arthritis of a large joint may follow brief attacks. Chronic progressive arthritis not preceded by brief attacks, chronic symmetric polyarthritis, arthralgias, myalgias and fibromyalgia syndromes are not criteria for musculoskeletal involvement.

**Indications for specific serologic testing**

Serologic testing is indicated in patients with erythema migrans and in those with signs of disseminated Lyme disease and a history of erythema migrans or of exposure in an endemic area.

The collection of sequential serum samples from patients with erythema migrans in areas not known to have Lyme disease can be of diagnostic value and can help to define the geographic distribution of the disease.

Chronic fatigue and fibromyalgia without objective signs of Lyme disease are not considered to be manifestations of the disease and should not prompt serologic testing.

The determination of appropriate quantitative CSF antibody levels may be useful for patients with possible neurologic disease; however, tests to accomplish this are currently unavailable in Canada.

**Interpretation of positive test results**

To interpret serologic test results with the use of currently available methods one must consider the signs and symptoms of the patient and whether he or she has been in an area known to have Lyme disease. In nonendemic areas most positive test results will be falsely positive unless there is a very high clinical suspicion of Lyme disease. A positive result will confirm illness in a patient with erythema migrans, or a history of it, and other typical manifestations of Lyme disease.

A positive test result in an asymptomatic patient is of no diagnostic value. Such a result in a patient with atypical symptoms does not necessarily imply evidence of the disease.

**Guidelines for treatment**

The following guidelines apply for the treatment of erythema migrans, Bell's palsy without CSF abnormalities and first-degree heart block.

- **Adults:** Doxycycline (100 mg orally twice daily for 2 to 3 weeks) or amoxicillin (500 mg orally three times daily for 2 to 3 weeks) plus probenecid (same dosage as for amoxicillin).
- **Children:** Amoxicillin (40 mg/kg daily in three oral doses for 2 to 3 weeks) plus probenecid (same dosage as for amoxicillin).

The guidelines for the treatment of central nervous system disease with CSF abnormalities, second-degree or third-degree atroventricular block and arthritis are as follows.

- **Adults:** Ceftriaxone (2 g intravenously once daily for 2 weeks).
- **Children:** Ceftriaxone (50 mg/kg every 12 hours intravenously or intramuscularly for 2 weeks).

Doxycycline should not be given to pregnant women or children less than 9 years old. Erythromycin can be used, but it has been found to have less clinical effectiveness.

**Treatment outcomes**

Treatment is effective in 95% to 100% of cases of erythema migrans, in 90% to 95% of cases of other acute manifestations and in 80% to 85% of those of chronic disease.

Herxheimer's reaction occurs in 15% to 30% of cases but is usually mild and can be treated with nonsteroidal anti-inflammatory drugs.

Postinfectious fatigue syndromes may occur in approximately 15% of treated patients but usually resolve spontaneously in 6 to 12 months.

In the absence of objective signs of Lyme disease, treatment is rarely useful. In these situations the potential risks associated with treatment may outweigh any potential benefits. The most frequent reason for treatment failure is misdiagnosis; other diagnoses should be considered in such situations.

**Laboratory investigation**

Definitive laboratory diagnosis of Lyme disease in humans depends on the detection of *B. burgdorferi* or adequate serologic evidence of infection. Current serologic tests lack sensitivity and specificity and show a high degree of variability. For these reasons an effective reference service is essential. Serologic tests are indicated only for those people who have travelled to endemic areas or have signs and symptoms compatible with Lyme disease. Moreover, serologic findings may be negative early in the disease. Antibody formation may be stopped with early treatment or may persist after adequate treatment. The appropriate use of serologic diagnostic tests in highly suspect cases will minimize misinterpretation of the results. It is expected that the limitations of current methods will be overcome by
new and emerging ones that will greatly improve the reliability of serologic testing.

**Standardization and use of laboratory tests**

All laboratories in Canada should use ELISA kits (from a commercially available source) for initial testing of both IgG and IgM antibodies to *B. burgdorferi*.

Additional diagnostic tests such as IFA may be used as an adjunct to ELISA.

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

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

When neuroborreliosis is suspected routine biochemical and cytologic examination of CSF is indicated. Reliable specific antibody testing of CSF is not generally available at present.

The Western blot technique should be used to confirm the presence of specific antibodies detected in sera by the initial ELISA. Some false-positive results may be ruled out by the Western blot technique. Standards for interpretation of the results must be developed.

A central reference laboratory should be adequately supported to perform proficiency tests and establish standards for reference reagents and to evaluate commercial products.

**Low-yield laboratory procedures**

Isolation of *B. burgdorferi* (from biopsy specimens of the advancing edge of erythema migrans lesions) or identification by means of immunospecific staining is encouraged when possible.

**Newer or less-common methods**

At this time methods for the laboratory diagnosis of Lyme disease, such as antigen detection by means of ELISA, lymphocyte transformation and detection of circulating immune complexes, are not appropriate for routine clinical diagnosis.

The development of the polymerase chain reaction and antibody detection assays based on synthetic peptide and recombinant proteins is encouraged.

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**Conferences continued from page 1622**

**Aug. 5–9, 1991**: 2nd International Congress on Amino Acids and Analogues
Vienna
Dr. Gert Lubec, Department of Paediatrics, University of Vienna, Währinger Gürtel 18, A 1090 Vienna, Austria; telephone 43-222-23-40-424 or 43-222-40-400-3229, fax 43-222-40-400-3238

**Aug. 9–11, 1991**: Federation of Medical Women of Canada Board of Directors Meeting and Educational Session (in conjunction with the 124th Annual Meeting of the CMA)
Sheraton Centre of Toronto
Federation of Medical Women of Canada, 106–1815 Alta Vista Dr., Ottawa, ON K1G 3Y6; (613) 731-1026

**Aug. 11–15, 1991**: International Symposium for Psychotherapy of Schizophrenia
Stockholm
Stockholm Convention Bureau, PO Box 6911, S-102, 39 Stockholm, Sweden

**Aug. 11–16, 1991**: Ontario Medical Association section meetings (in conjunction with the 124th Annual Meeting of the CMA)
Hilton International Toronto
Ontario Medical Association, 600–250 Bloor St. E, Toronto, ON M4W 3P8; (416) 963-9383, fax (416) 963-8819

**Aug. 14, 1991**: Canadian Medical Protective Association Annual Meeting (in conjunction with the 124th Annual Meeting of the CMA)
King Edward Hotel, Toronto
Canadian Medical Protective Association, Carling Square, 560 Rochester St., Ottawa, ON K1G 5K7; (613) 236-2100

**Aug. 18–23, 1991**: 5th Congress of the International Psychogeriatric Association
Rome (previously planned for Jerusalem)
Dr. M.O. Agbayewa, Riverview Hospital, Port Coquitlam, BC V3C 4J2, (604) 524-7038, fax (604) 524-7250; or Dr. M.R. Eastwood, Clarke Institute of Psychiatry, 250 College St., Toronto, ON M5T 1R8

**Aug. 23–25, 1991**: 2nd World Congress of Acupuncture and Natural Medicine (with precongress course Aug. 21 and 22 and postcongress course Aug. 26 and 27)
Conference Hall, Beijing International Convention Centre, Beijing
Steven K.H. Aung, chairman, 1210 First Edmonton Place, 10665 Jasper Ave., Edmonton, AB T5J 3S9; (403) 426-2760 or 426-2764

**Nov. 6–7, 1991**: National Conference on Childhood Injury Prevention — Working Together for a Safer World
Ottawa
Canadian Institute of Child Health, 55 Parkdale Ave., 3rd Floor, Ottawa, ON K1Y 1E5; (613) 729-3206, fax (613) 722-4829