

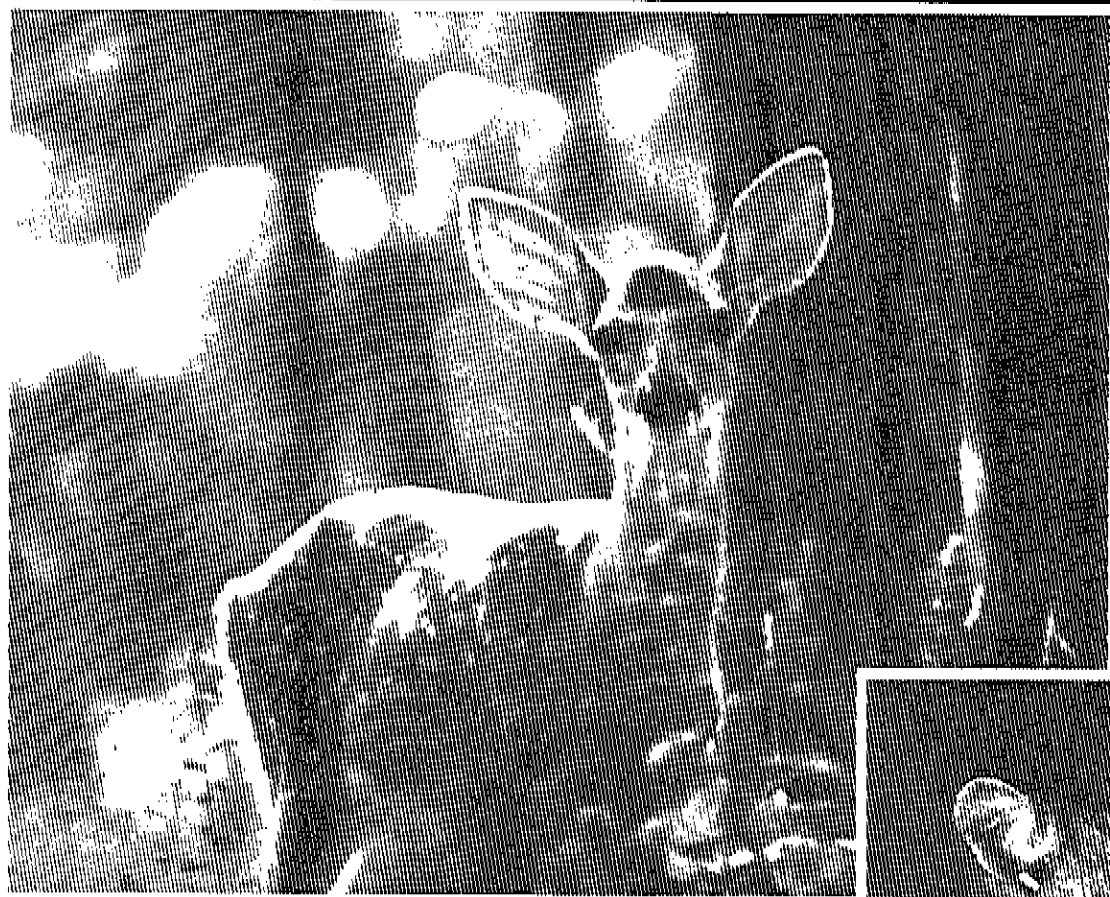
Ixodes scapularis :
principal vector of
B. burgdorferi in the
United States of America.



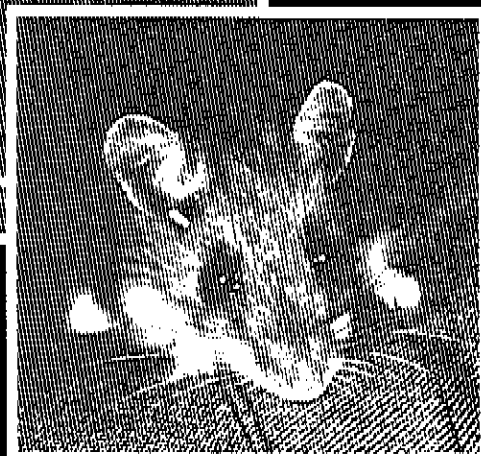
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R E P O R T O F A W H O W O R K S H O P O N L Y M E B O R R E L I O S I S

Piestany, Slovakia, 6 October 1993



White-tailed deer :
Principal maintenance
host of adult tick
Ixodes scapularis.



Peromyscus Leucopus
(white footed deer mouse):
Principal rodent reservoir of
Borrelia burgdorferi in
Eastern United States.



WORLD HEALTH ORGANIZATION

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CONTENTS

	<u>Page</u>
INTRODUCTION	2
1. LYME BORRELIOSIS SURVEILLANCE AND REPORTING	2
2. ZONOTIC ASPECTS OF LYME BORRELIOSIS	3
2.1 Etiology	3
2.2 Ecology of vectors and transmission	3
2.3 Reservoir and host animals	4
2.4 Diagnosis and identification of <i>Borrelia burgdorferi</i>	5
2.5 Research on Lyme borreliosis zoonotic aspects	6
2.5.1 Identification of host animals for ticks based on investigations of residual blood meals	6
2.5.2 Epidemiological investigation of dogs in the Brandenburg district of Germany	6
2.5.3 Research on immunological and molecular polymorphism of the major immunodominant outer surface proteins (Osp) A and C	6
3. CLINICAL PICTURE, TREATMENT AND CLINICAL PATHOLOGY	6
3.1 Clinical picture	6
3.2 Treatment	7
3.3 Clinical pathology	7
4. REDUCING THE RISK OF ACQUIRING LYME BORRELIOSIS	7
5. RESEARCH REQUIREMENTS FOR LYME BORRELIOSIS CONTROL	9
6. OVERALL CONCLUSIONS	10
Table 1 - List of major wild and domestic animal hosts for <i>B. burgdorferi</i> . .	11
Figures 1-5	12
ANNEX 1 - List of key-note speakers	16
ANNEX 2 - Case definition of Lyme borreliosis for surveillance and reporting systems in the United States of America	17
ANNEX 3 - Lyme disease case report form	19

INTRODUCTION

Dr T. Fujikura, Veterinary Public Health, WHO, thanked Professor E. Kmety and the Organizing Committee of the International Conference on Zoonoses, Piestany, for their provision of facilities to hold the Workshop, and opened the meeting on behalf of Dr Hiroshi Nakajima, Director-General of the World Health Organization.

Although the disease presently described as Lyme borreliosis was recognized as long ago as 1909, it is only in recent decades that outbreaks have occurred on an epidemic scale and been reported in many parts of the world, including Canada, many European countries, Japan and the USA. Very few cases were reported in Australia. The infection has occurred not only in man but also in many animal species such as cattle, horses, dogs, deer among others. However, the zoonotic aspects of Lyme borreliosis have not so far been clearly defined, particularly (1) epidemiology, including the transmission cycle from *Ixodes* ticks to human and animal populations, (2) occurrence of the disease, especially in relation to ecology of the vectors, and (3) prevention and control measures as well as related areas of diagnosis and treatment.

The Workshop was convened to discuss the zoonotic aspects of the disease and improvements in diagnostic methods common to man and animals, surveillance, prevention and control measures in human and animal populations at risk. Working teams should be formed on the various zoonotic aspects for international cooperation within the WHO context of health for all.

Dr Fujikura described WHO's activities in this field since the early 1980's, through various programmes including the former Biological Vector Control programme, Microbiology and Immunology Support Services and the Veterinary Public Health programme. The WHO Regional Office for Europe had organized two meetings, namely the WHO Workshop on Lyme borreliosis in Europe, Baden, June 1987, and the WHO Workshop on Lyme borreliosis, Stockholm, June 1990 to discuss an inter-laboratory study with the participation of 26 institutions in 12 countries, and a WHO Collaborating Centre for Lyme Borreliosis had been established in Prague in 1989. In addition, the Veterinary Public Health programme was supported in its activities through communications and other contributions made by Professor A. Speilman, Boston, USA, and several other world recognized experts.

Professor R.C. Johnson was appointed overall Moderator of the Workshop.

1. LYME BORRELIOSIS SURVEILLANCE AND REPORTING

Although the disease presently called Lyme borreliosis was recognized at the beginning of the century, the epidemiological situation was not truly studied until an unusual cluster of juvenile arthritis cases was found in Lyme, Connecticut, USA in the early 1970's; skin rash, Erythema migrans (EM), chronic skin diseases and neurological symptoms were also identified as acute and chronic symptoms and was from then on called "Lyme disease". In 1982 *Borrelia burgdorferi* was isolated from *Ixodes scapularis* (*I. domini*) and identified as the cause of Lyme disease/Lyme borreliosis which is now widely found in Asia, Canada, some European countries, Japan, and the USA. Surveillance and monitoring systems at the national level are increasingly important for determining the magnitude of public health consequences of Lyme borreliosis as well as for development of prevention and control strategies.

Systematically organized surveillance is essential in research on the epidemiology of Lyme borreliosis and can provide guidance for prompt public health action. In this context, definition of a "Lyme borreliosis-case" based on clinical manifestations of the disease may require further improvement. Complete anamneses results of clinical examination, complemented with highly specific laboratory tests are necessary to securely characterize Lyme borreliosis cases for disease reporting. As a result of the elaboration of an improved standardized case definition (Annex 2) of Lyme borreliosis, the disease has now become notifiable in 49 US States (Annex 3).

The Centers for Disease Control (CDC), Atlanta, USA, has also developed a surveillance system on Lyme borreliosis. This system provides information such as spatial distribution of Lyme borreliosis (Fig. 1), intensity of natural cycles of the disease, and geographical spread of *I. scapularis* and *I. pacificus* (Fig. 2). The surveillance system facilitates identification of the public health impact and the development of control strategies in the areas at risk, although it still requires essential funding for present and long-term efforts.

2. ZONOTIC ASPECTS OF LYME BORRELIOSIS

2.1 Etiology

The causal agent of Lyme borreliosis is *B. burgdorferi*, a new species of *Borrelia*. It has the basic structural features that are characteristic of *Spirochetes*.

Borrelia are unique among the *Spirochetes* in their arrangement of DNA. *B. burgdorferi* has a linear chromosome and linear plasmids in addition to the typical supercoiled variety. One or more of the plasmids appears to be associated with the virulence factors.

2.2 Ecology of vectors and transmission

The following four species of *Ixodes ticks* are recognized as vectors of *B. burgdorferi*, to human beings: *I. scapularis* and *I. pacificus* (new world); and *I. ricinus* and *I. persulcatus* (old world). These species are of similar general morphology. They require relatively high humidity when separated from the host animal. The ticks inhabit woodland, moorland and woody or brushy pastures. They also go through similar life cycles in the egg and three motile feeding stages. Each tick feeds on three different animals as a larva, a nymph, and an adult, respectively. Generation time amounts to about two years, perhaps less in warmer climates or as long as 5-6 years in northern latitudes. A tick spends most of its lifetime in soil or vegetation. The duration of feeding on host animals is not more than three weeks; females drop to the ground where they lay 2000-3000 eggs in a single cluster.

The above-mentioned ticks can parasitize a multitude of species (e.g. *I. ricinus* can parasitize at least 237, *I. persulcatus* 212, *I. scapularis* 119, and *I. pacificus* 80 species). In the USA the white-footed mouse (*Peromyscus leucopus*) is an important host of *I. scapularis* (larva and nymph). Sub-adults of *I. pacificus* preferably feed on lizards. Larvae of *I. ricinus* can feed on *Apodemus* and other rodents. The nymph tends to feed on rodents, lizards, birds, squirrels and hares. Deer are important host animals for adults of all four *B. burgdorferi* vector species. Sub-adults of *I. scapularis*, *I. ricinus* and *I. persulcatus* are possibly carried long

distances by migrating birds from spring to autumn. Throughout the feeding stage ticks can also feed on humans.

The above four species of *Ixodes* are distributed over vast areas of the northern hemisphere; one old world species is found from Japan to England and overlaps with a new world species in the vicinity of 50°-55° longitude. In the Americas, *I. pacificus* is distributed along the Pacific coast from British Columbia to southern California, including areas of western States.

Other species of ticks and biting insects such as tabanids, mosquitoes and fleas may be involved secondarily in transmission of *B. burgdorferi*.

Transmission

The risk of *B. burgdorferi* infection in humans depends upon (1) the number of infected vectors and (2) the number of reservoirs in the environment. Primary vectors are *I. scapularis* in north central and north eastern USA, *I. pacificus* in western USA, *I. ricinus* and *I. persulcatus* in Europe and Eurasia.

Other species of *Ixodes* do not feed on humans but can maintain endemic foci in nature. *Ixodes* ticks feed on a broad range of mammals as well as birds. Blood is the sole nutrient and there is only one feed for each development stage. Rodents are considered as primary reservoir hosts for immature stages (larva/nymph) of the ticks. Adult ticks feed on larger mammals, preferably deer. *Borrelia* remain in the ticks during the evolution to the subsequent stage and can be transmitted to the next hosts on which they feed. Adult ticks have two opportunities to feed on an infectious blood meal; their infection rate is almost double that of the nymph stage (10-30%) in endemic foci.

For effective transmission of *Borrelia* to the host, *Ixodes* needs to be attached for approximately 40 hours to the host. In the USA, June/July is the active stage of the nymph of *I. scapularis*. In central Europe, *I. ricinus* shows one active peak from April-June and a second peak from late August through September. The feeding pattern is also modified by climatic conditions. A unimodal feeding pattern is observed in a cool, moist season, while bi-modal activity is favoured under warm, dry conditions. *Ixodes* ticks are generally found in forest areas where host animals live in a cool, moist micro-climate. Establishment of new endemic foci may be facilitated by migrating birds.

2.3 Reservoir and host animals

There is extensive exposure of animals to *B. burgdorferi* in Lyme disease foci. *Borreliae* have been isolated or detected in three species of rodents in Europe, and from one species of rodent in Japan. In the USA, *Borrelia* have been isolated from or detected in at least 18 wild mammals, three domestic mammals and eight birds. White-footed mice are particularly important as chief reservoirs in north eastern and north central USA. The ingestion and transmission of *B. burgdorferi* by *I. scapularis* in northern USA are favoured by the seasonal appearance of nymphs before larvae. Larvae often feed on mice which had been previously parasitized by nymphs. Some mammals, such as white-tailed deer (*Odocoileus virginianus*), which are extensively parasitized by *I. scapularis*, are apparently incompetent as reservoirs.

Birds also harbour *B. burgdorferi*. These bacteria have been isolated from at least eight bird species, from larval *I. scapularis* feeding on several species, detected in *I. ricinus* feeding on birds on an isolated island in the Atlantic ocean. Some birds, such as the common grackle (*Quiscalus guiscula*) have been reported to be reservoir incompetent; similarly reptiles are apparently incompetent hosts for the *Spirochetes*.

The relatively high prevalence of competent mice infected with *B. burgdorferi* in north eastern USA is largely responsible for the relatively high infection rate of *I. scapularis*, reported as being from 12-100%. In contrast, infection rates of 3% or less have been reported for adult *I. pacificus* where hosts of predilection for immature ticks are reservoir-incompetent western fence lizards (*Sceloporus occidentalis*).

A list of major wild and domestic animal hosts for *B. burgdorferi* is given in Table 1.

2.4 Diagnosis and identification of *B. burgdorferi*

The diagnosis of Lyme borreliosis in patients should be based on the clinical picture and serology used to confirm the clinical diagnosis. Presence of antibodies (Ab) generally indicates previous exposure to the *Spirochetes*. Furthermore, false-positive or false-negative results may occur.

Present technology and methods are as follows:

- (1) Isolation of *B. burgdorferi* from patients serves for direct diagnosis. Isolation from biopsied materials derived from the characteristic expanding red skin lesions, Erythema migrans (EM), is the most efficient technique. Even though *B. burgdorferi* has also been isolated and successfully subcultured from the blood, cerebrospinal fluid and synovial fluid, these investigations were shown to be less sensitive than isolations from skin biopsy specimens. After adequate antimicrobial treatment *B. burgdorferi* cannot be isolated from the site of the original EM lesion.
- (2) Detection of Ab to *B. burgdorferi* is the best and most commonly used method for the laboratory diagnosis of Lyme borreliosis. Immunoblotting is a useful technique for verifying results obtained with enzyme-linked immunosorbent assay (ELISA) or Indirect immunofluorescent assay (IFA). Prolonged IgM response in Lyme borreliosis and sustained IgG response were detected for many years after "successful treatment". Therefore, a persistent positive titre after treatment does not necessarily indicate failure of treatment or the continued presence of *B. burgdorferi*. Somewhat delayed immunoresponse after contact to *B. burgdorferi* can lead to a negative Ab test in the early phase of the disease.
- (3) Polymerase chain reaction (PCR) holds the greatest potential for a rapid, sensitive, specific and direct method for determining *B. burgdorferi* in patient specimens. It is not yet commercially available.

2.5 Research on zoonotic aspects of Lyme borreliosis

2.5.1 Identification of host animals for ticks based on investigations of residual blood meals (WHO/FAO Collaborating Centre for Research and Training in Zoonoses and Foodborne Diseases, Berlin, Germany)

Enzyme immunoassay (EIA) was developed at this Centre to identify host animals of *Ixodes* ticks and to determine competence for *B. burgdorferi*. Two hundred tick samples collected in the field were examined:

- (1) Animal species identified and prevalence of borrelia positive ticks (nymph/adult, male/female) are shown in Fig. 3.
- (2) Animal species identified by investigating residual blood meals in ticks and rate of *Borrelia* carriage is shown in Fig. 4.

Ixodes ticks grow with blood meals from various species of wild animal hosts. *B. burgdorferi* is found in these hosts (including squirrels, crows, deer, rabbits, wild boar, foxes and mice) and transmitted to *Ixodes* ticks which remain the potential source of Lyme borreliosis infection to humans and domestic animals.

2.5.2 Epidemiological investigation of dogs in the Brandenburg district of Germany (WHO Collaborating Centre for Research and Training in Veterinary Public Health, Hanover, Germany)

Surveillance and monitoring of the antibody prevalence of *B. burgdorferi* in dog populations may provide an indicator for potential environmental risk to the human population. Risk factors for canine seropositivity may directly or indirectly illuminate certain aspects of the epidemiology of human Lyme borreliosis.

Surveillance based on EIA was carried out in the Brandenburg district. Some areas indicated that 30-40% of dogs were serologically positive, while other areas remained at relatively lower levels (Fig. 5). The public health consequences of the disease in this region require further study.

2.5.3 Research on immunological and molecular polymorphism of the major immunodominant outer surface proteins (Osp) A and C (Max von Pettenkofer Institute, University of Munich, Germany)

Osp of *B. burgdorferi* play a crucial role in diagnosis and vaccine development. The Institute's investigations indicate that OspC is closely related to early immune response of Lyme borreliosis in humans and this has important implications for development of future diagnostic reagents and vaccines.

3. CLINICAL PICTURE, TREATMENT AND CLINICAL PATHOLOGY

3.1 Clinical picture

Once the tick has injected the *Spirochete* into the host it may spread locally in the skin or be disseminated systemically via the blood or lymph. In humans, the presence of *B. burgdorferi* in the skin results in the characteristic expanding red skin lesion, EM, 7-9 days following the tick bite. The EM may be associated with headache, stiff neck, migratory pain in muscles and joints, cardiac abnormalities, meningitis and cranial and peripheral neuropathies. Months after onset of disease, brief attacks of

arthritis occur usually involving large joints, especially the knee. The arthritis may persist for several years and become chronic in a small percentage of patients. Chronic neurological disease affecting the peripheral or central nervous system may occur, sometimes following years of latent infection. Arthritis is common in the USA whereas neurological involvement is most frequently observed in Europe. Limited information is available about the disease manifestations in Asia. *Acrodermatitis chronica atrophicans*, which is primarily observed in Europe, is an excellent example of the ability of *B. burgdorferi* to persist in the host. The skin lesion usually begins with a swollen, bluish-red discoloration of the skin on an extremity. Atrophy of the skin occurs as a result of an inflammatory phase that may persist for many years. The *Spirochete* has been cultured from these lesions as long as 10 years after their onset.

3.2 Treatment

Antimicrobials are effective in the treatment of Lyme borreliosis in most patients. However, efficiency of treatment varies with the stage and manifestations of the disease. Early Lyme borreliosis patients and those with arthritis generally respond well to oral doxycycline or amoxicillin therapy. Intravenous therapy is necessary for patients with objective neurological or cardiac abnormalities or for patients who have failed oral therapy. Ceftriaxone, cefotaxime and high-dose penicillin are used most often for this purpose.

3.3 Clinical pathology

B. burgdorferi is a highly invasive extra-cellular pathogen. It migrates through the endothelial cell monolayer and can penetrate the central nervous system. A characteristic of Lyme borreliosis is the paucity of *Spirochetes* in the infected organs. However, the clinical manifestations are associated with the presence of living *Spirochetes* which are few in number whether the illness is acute or chronic. The favourable response to antimicrobial therapy supports this relationship. However, some exceptions to this are patients with chronic arthritis who do not respond to antimicrobial therapy; such arthritis could also be considered as a result of a complex immune response related to Lyme borreliosis.

The inflammatory response elicited by *B. burgdorferi* primarily consists of mononuclear cells with the exception of the synovial fluid where granulocytes predominate. The most common histological pattern associated with infected tissues is an infiltrate of lymphocytes and plasma cells. The pathology associated with Lyme borreliosis is caused by relatively few *Spirochetes* suggesting the existence of additional mechanisms for the amplification of their pathogenicity. One possible mechanism may be the release of cytokines from host cells.

Clinical diagnosis of Lyme borreliosis can be established by correctly identifying its characteristic cutaneous marker, EM. This is particularly important since serological tests are not reactive during the first few weeks of illness, a time when EM lesions are most likely to be present.

4. REDUCING THE RISK OF ACQUIRING LYME BORRELIOSIS

Humans encounter ticks in forests, transitional vegetational zones, pastures, parks, lawns surrounding homes, brush-like and woodland areas bordering lawns, and even in houses after dogs and cats have carried ticks inside. The risk of acquiring Lyme borreliosis can be reduced through

personal protection measures or by efforts aimed at reducing the number of ticks. Human vaccines are not currently available.

(1) Personal protection measures to prevent tick bites and to locate and promptly remove attached ticks are effective and include:

- wearing light-coloured clothing so that crawling ticks are more visible and easily removed;
- tucking one's trousers into socks and tucking one's shirt into trousers to help prevent crawling ticks from gaining access to the body surface;
- walking in the centre of woodland trails so as to reduce exposure to host-seeking ticks;
- frequently examining one's clothing, arms, neck and legs for ticks and removing them;
- thoroughly examining one's body when inside again and removing all attached ticks.

Ticks may be removed by grasping them firmly as close as possible to the skin with a pair of tweezers and steadily pulling them away from the skin. An antiseptic may be applied to the sites of attachment; the ticks may also be saved for identification and testing.

(2) Chemical repellent may be applied to skin and clothing to provide added protection from tick bites. Permethrin applied to clothing causes rapid unconsciousness and death of ticks. Standard repellents (such as N,N-diethyl-m-tolamide) repel rather than kill ticks and can be impregnated into clothing or applied to the skin. More study is needed to find improved and more effective chemical repellents.

(3) Elimination of crucial host animals, or modification of the environment have been successful in reducing the number of ticks, but both have limitations. Deer are a crucial host for maintaining dense populations of *I. scapularis*, and reduction of the number of deer to a very low level, or use of fencing to exclude deer, have also reduced the number of ticks.

(4) Burning bushes and keeping grass short in gardens/yards have also reduced the number of ticks. Burning destroys many host-seeking ticks and generally makes the habitat inhospitable for egg-laying, hatching, and moulting. Burning may also reduce the number of host animals but the effects of burning can be complex and occasionally even result in increased number of tick bites. Sociological and safety reasons will limit the use of burning as a preventive measure.

(5) Properly timed and applied insecticide/chemical acaracides can significantly reduce the number of ticks in yards/gardens and wooded environments. Time of application will vary with tick species and the climatic zone.

(6) Vaccination feasibility was demonstrated by the successful, active immunization of hamsters with killed *B. burgdorferi* cells, and these results were the basis of an effective vaccine for dogs. Initial efforts to find a human vaccine have focused on recombinant DNA products. Phase I human trials are being conducted with OspA lipoprotein. There are concerns about the use

of a single component vaccine, especially in Europe where considerable heterogeneity in the expression and antigenic composition of OspA occurs.

5. RESEARCH REQUIREMENTS FOR LYME BORRELIOSIS CONTROL

(1) In addition to the three recognized species of the genus *Borrelia*, namely, *B. burgdorferi* (sensu stricto), *B. garinii* and *B. afzelii* (group VS 461), there is an independent species isolated from *Ixodes ovatus* requiring a new species name. Differentiation of species within the genus *Borrelia* should be based on reactivity to monoclonal antibodies (Ab), genomic DNA homology, and restriction fragment length polymorphism (RFLP) analysis. Ecology of vectors and reservoirs should also be a basis for classification of the genus *Borrelia*. However, further research is required in these areas.

(2) Overall diagnostic methods for borreliosis should be standardized with the highest possible levels of sensitivity and specificity, including:

- i. dark-field microscopy, Giemsa, Carbol-fuchsin staining, and silver impregnation to be applied to cerebrospinal fluid, blood, liver, kidney and other tissues and cultures;
- ii. direct and indirect immunofluorescence tests for detection of borrelia in ticks and immunoperoxidase staining for skin biopsies;
- iii. methods for preparation of Osp A and B (OspA, 30-32 KDa, OspB, 34-36 KDa) and OspC (21-22 KDa);
- iv. although IFA, indirect haemagglutination assay, EIA and Western blot are commonly used and may require further standardization, recombinant flagelin antigens, OspA, OspC, and 39 KDa protein should be standardized with regard to application as EIA antigens;
- v. PCR for detection of genes of chromosomal origin would be useful for diagnosis as well as epidemiological studies;
- vi. although *Borreliae* are cultivable for isolation and antigen production in BSKII medium as well as CMRL medium, a more simple and economical growth medium should be developed for these purposes.

(3) There is an urgent need to establish a worldwide network for Lyme borreliosis surveillance including geographical distribution of *Ixodes* vectors, species and distribution of reservoir animals, and morbidity/mortality in humans and animals in endemic areas.

(4) The initiation of national reporting systems and control programmes should be encouraged. Additional WHO collaborating centres should be established for providing epidemiological information, reference materials, diagnostic reagents and methodology, as well as promoting/initiating research in epidemiology, vector control and identification of reservoirs in endemic areas. These centres should also serve as consultative centres for all aspects of prevention and treatment of the disease in endemic areas.

(5) Scientific groups working on vaccine development and related research should be encouraged to study whole cell vaccine, recombinant candidate vaccines such as OspA, OspC and others. Animal models for immunological research and vaccine development are also urgently needed.

(6) Research should focus on specific areas such as: immunology, pathogenicity of *B. burgdorferi*, molecular biology, epidemiology, vector biology and reservoirs responsible for epidemics. With regard to clinical aspects, protocols are to be developed for diagnosis, treatment, prognosis and rehabilitation.

6. OVERALL CONCLUSIONS

(1) Scientists all over the world are called on for close cooperation and participation in global activities against Lyme borreliosis through the priority areas outlined above. In this connection, WHO, in close cooperation with other organizations such as FAO and OIE, should accept to act as a liaison body in development of research and control of this disease, in line with the aim of health for all by the year 2000.

(2) The group agreed that research on the zoonotic aspects of Lyme borreliosis would contribute to risk assessment, the management of public health consequences and control of the disease. This research may be achieved through internationally organized teams involving areas such as epidemiology and surveillance, including identification and control of reservoirs, vectors, and host animals transmission and reporting systems;

(3) Promoting international cooperation with organizations such as FAO, OIE, UNEP and other international institutions is important. The VPH unit of WHO should be the focal point of these activities. The WHO Collaborating Centre for Reference and Research in Lyme Borreliosis, Prague, is encouraged to play an increased role internationally by training scientists as well as initiating research projects and organizing meetings.

ACKNOWLEDGEMENTS

The secretariat of the Workshop wishes to express its sincere thanks to the following scientists for presenting papers, joining in the lively discussions and otherwise contributing to the meeting's success:

Dr P. Rosa (Hamilton, USA), Drs F. Matelscka, G. Khanakha, I. Slavic and M. Konadas (Slovak Republic) and Drs F. Tremel and P. Zeman (Czech Republic).

TABLE 1. WILD AND DOMESTIC ANIMAL HOSTS FOR *B. burgdorferi*¹

Common name	Scientific name
North America	
White-footed mouse	<i>Peromyscus leucopus</i>
Meadow vole	<i>Microtus pennsylvanicus</i>
Eastern chipmunk	<i>Tamias striatus</i>
Woodland jumping mouse	<i>Napaeozapus insignis</i>
Dusky-footed wood rat	<i>Neotoma fuscipes</i>
California kangaroo rat	<i>Dipodomys californicus</i>
Bushy-tailed wood rat	<i>Neotoma cinerea</i>
Pinon mouse	<i>Peromyscus truei</i>
Raccoon	<i>Procyon lotor</i>
White-tailed deer	<i>Odocoileus virginianus</i>
Columbian black-tailed deer	<i>Odocoileus hemionus</i>
Axis deer	<i>Axis axis</i>
Fallow deer	<i>Dama dama</i>
Black-tailed jackrabbit	<i>Lepus californicus</i>
Cottontail rabbit	<i>Sylvilagus floridanus</i>
Coyote	<i>Canis latrans</i>
Black bear	<i>Ursus americanus</i>
Dog	<i>Canis familiaris</i>
Horse	<i>Equus caballus</i>
Cow	<i>Bos taurus</i>
Veery	<i>Catharus fuscescens</i>
Northern mockingbird	<i>Mimus polyglottos</i>
Gray catbird	<i>Dumetella carolinensis</i>
Prairie warbler	<i>Dendroica discolor</i>
Orchard oriole	<i>Icterus spurius</i>
Common yellowthroat	<i>Geothlypis trichas</i>
American robin	<i>Turdus migratorius</i>
House wren	<i>Troglodytes aedon</i>
Europe	
Woodmouse	<i>Apodemus sylvaticus</i>
Yellow-necked mouse	<i>Apodemus flavicollis</i>
Bank vole	<i>Clethrionomys glareolus</i>
Asia	
Mouse	<i>Apodemus speciosus</i>

¹ Table provided and updated with the following information by Dr J.F. Anderson, New Haven, USA: - North America: deer mouse (*Peromyscus manicutatus*), Mexican wood rat (*Neotoma mexicana*), short-tailed shrew (*Blarina brevicauda*), song sparrow (*Melospiza melodia*); Europe: razorbill (*Alca torda*).

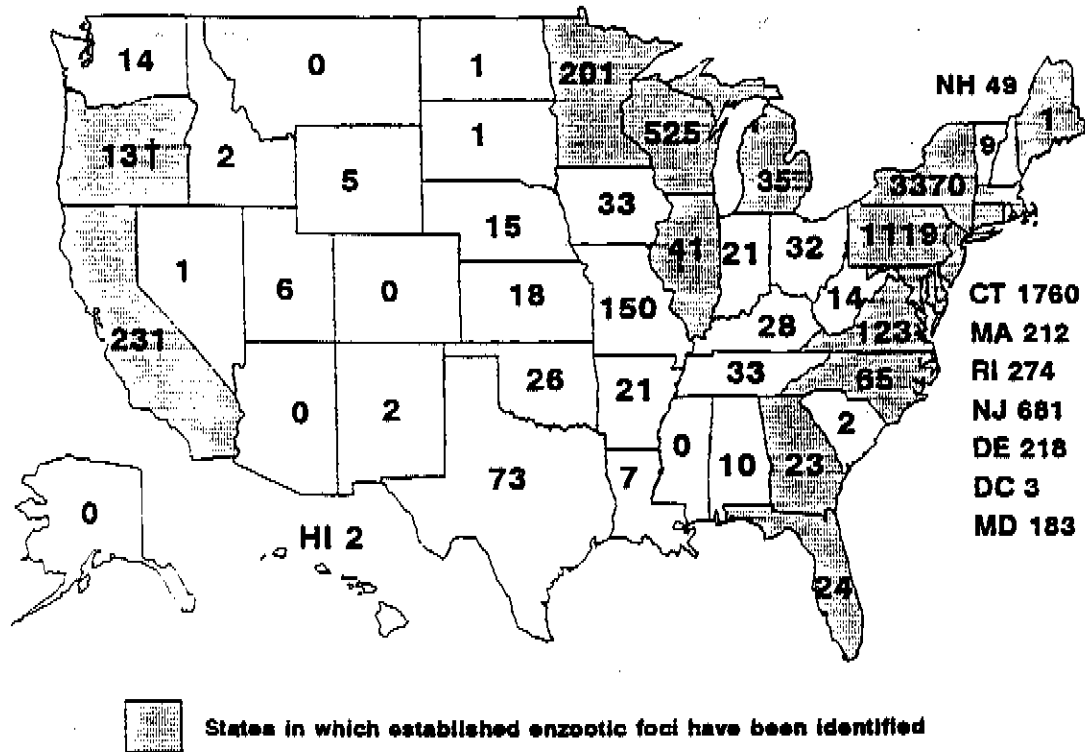
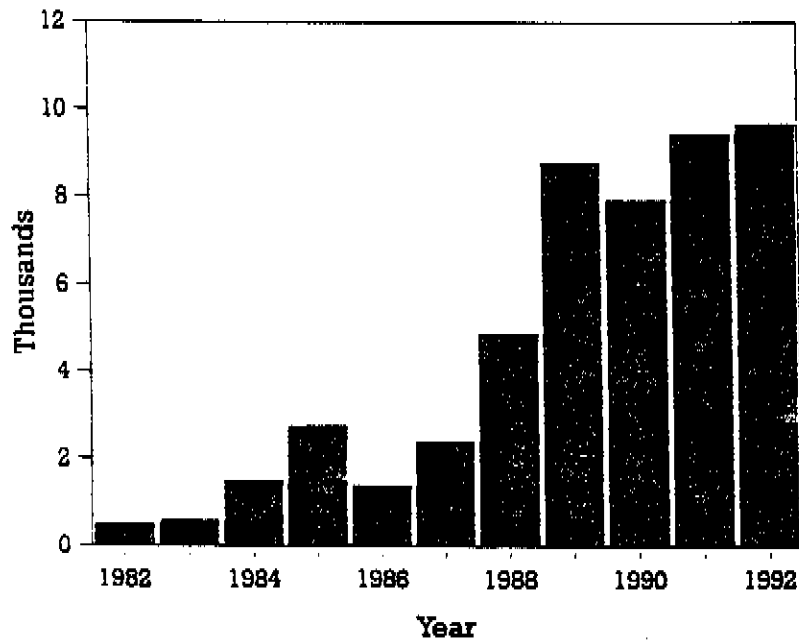


Fig.1. Distribution of enzoitic foci by State (above) and annual occurrence of Lyme borreliosis in the USA (below)



Distribution of Principal Vectors of Lyme Disease in Endemic Areas of the United States

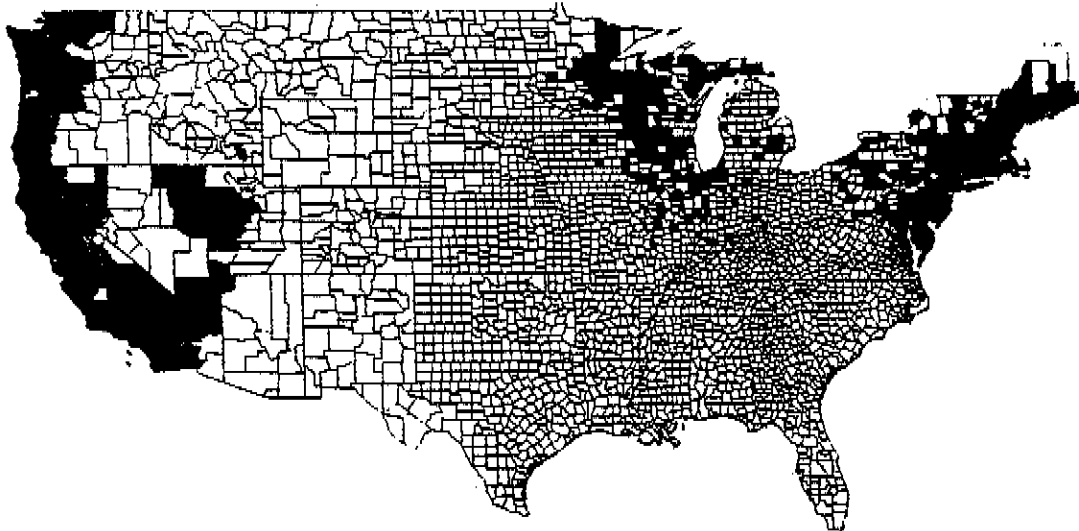
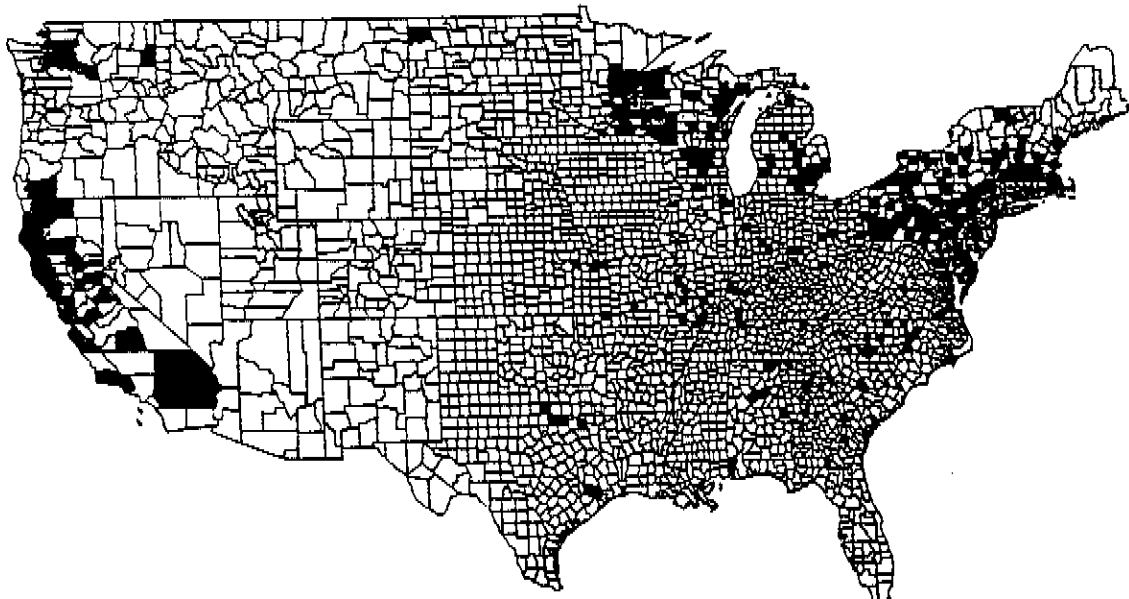


Fig. 2. Distribution of vectors (above) and human Lyme borreliosis occurrence in the USA (below).

Numbers of Cases Meeting CDC Case Definition By County, 1990



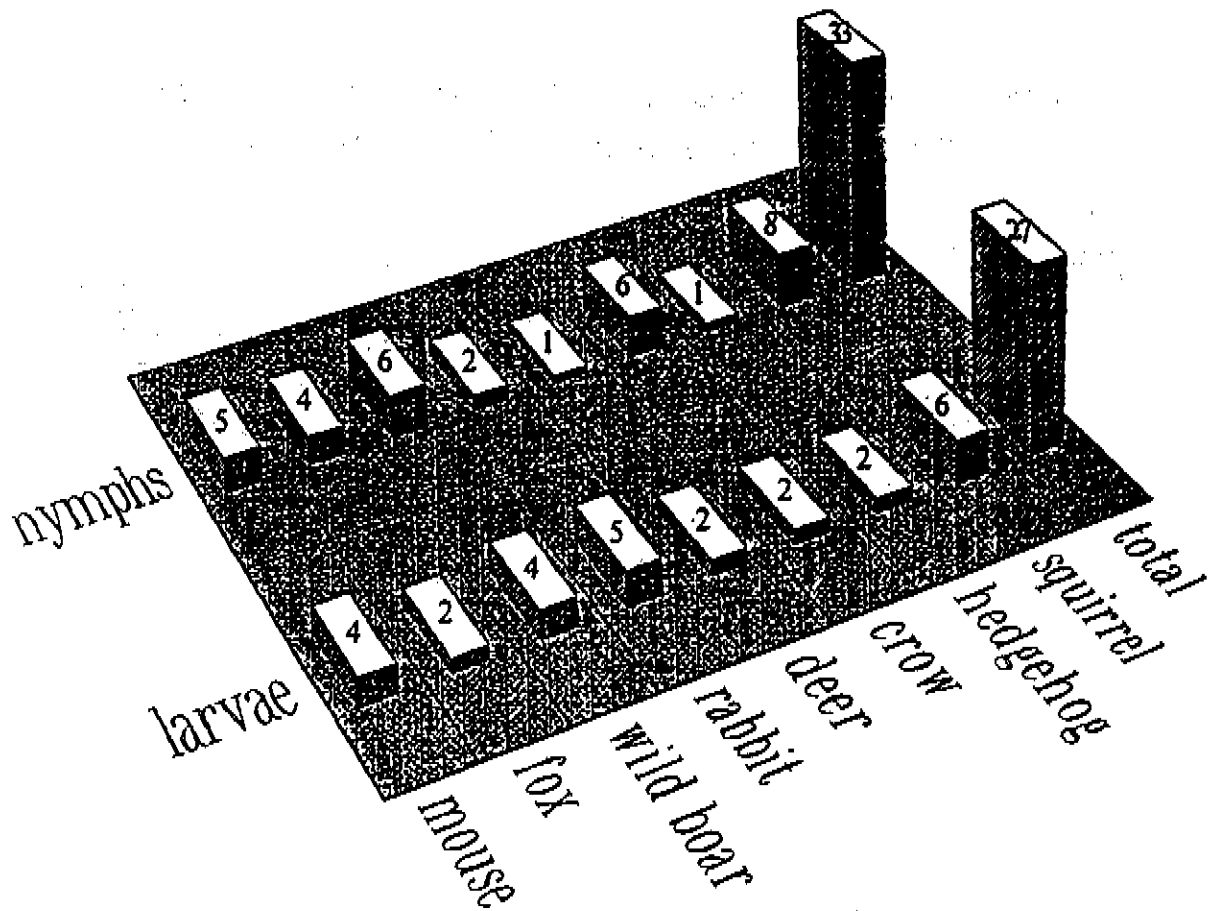
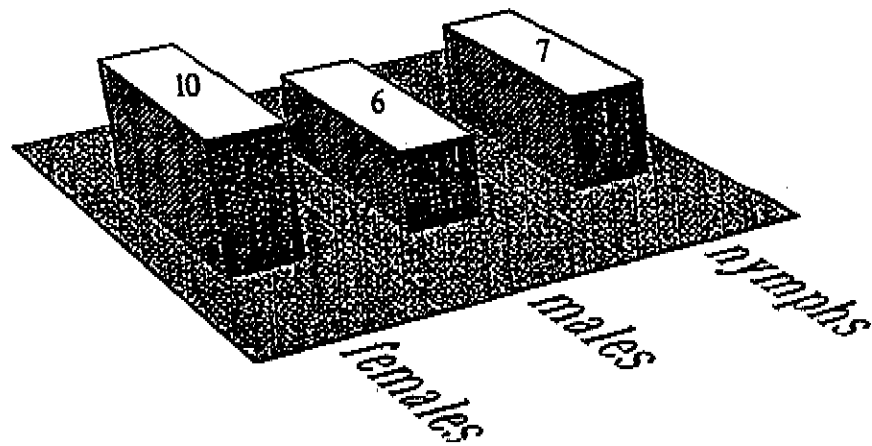


Fig.3. Percentage of identified animal species from a blood meal in the nymph or larva stage of *Ixodes* ticks (above), and percentage of *borrelia*-positive in nymphs and adults (females/males) of *Ixodes* ticks (below)



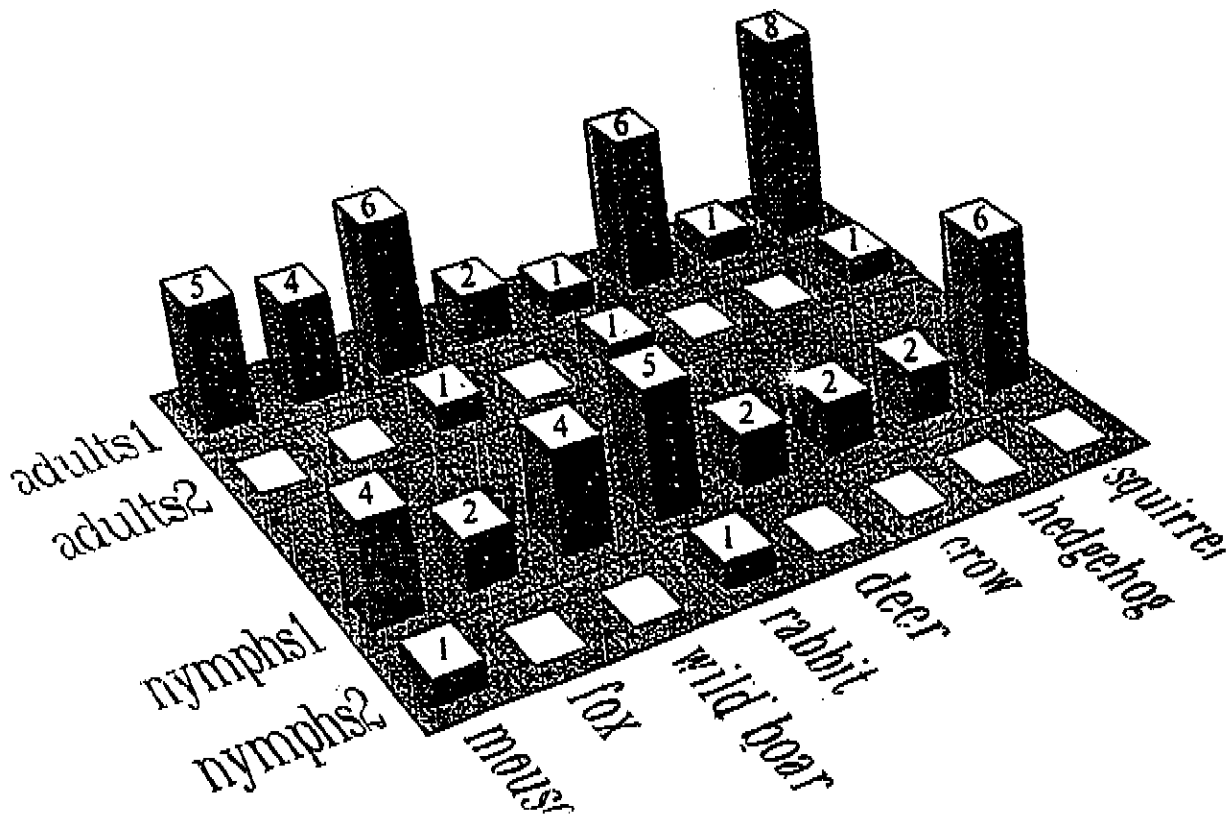


Fig.4. Identified animal species from blood meals taken during nymph or adult stage of *Ixodes* ticks, and ratios of *borrelia* carriage (2) to non-carriage (1) ticks.

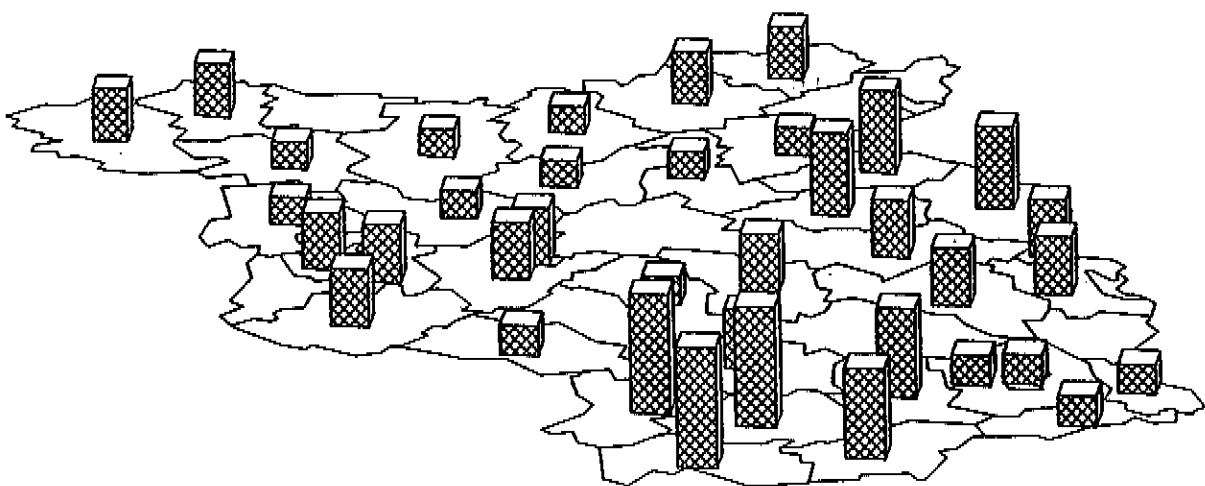


Fig.5. Seroprevalence in dogs in the districts of the Federal State of Brandenburg (highest prevalence = 40%)

ANNEX I

LIST OF KEYNOTE SPEAKERS

Dr J.F. Anderson, Department of Entomology, The Connecticut Agricultural Experiment Station, P.O. Box 1108, New Haven, Connecticut 06504, USA

Dr T. Dennis, Bacterial Zoonoses Branch, Centers for Disease Control, Vector-borne Infectious Diseases, P.O. Box 2087, Foothills Campus, Fort Collins, CO 80522, USA

Dr Dagmar Hulinska, National Institute of Public Health, Srobarova 48, 10042 Prague 10, Czech Republic

Dr A. Käsbohrer, WHO Collaborating Centre for Veterinary Public Health, Hanover School of Veterinary Medicine, Bischofsholer Damm 15, D-30559 Hanover, Germany

Professor E. Kmety, Department of Epidemiology, Medical Faculty of the Komensky Institute, Spitalska 24, 81108 Bratislava, Slovakia

Professor R.C. Johnson, Department of Microbiology, University of Minnesota Medical School, P.O. Box 196 UMHC, 1460 Mayo Memorial Building, 420 Delaware Street S.E., Minneapolis, MN 55455-0312, USA (Moderator)

Dr A. Schönberg, Institute of Veterinary Medicine, Robert von Ostertag Institute, Diedersdorfer Weg 1, D-12277 Berlin, Germany

Dr Bettina Wilske, Pettenkofer Institute, Munich University, 9a Pettenkoferstrasse, D-80336 Munich, Germany

Professor Y. Yanagihara, Department of Microbiology, Faculty of Pharmacological Sciences, Shizuoka University, 52-1 Yada, Shizuoka City, 422 Japan

WHO Secretariat

Dr O. Cosivi, Associate Professional Officer, Veterinary Public Health, Division of Communicable Diseases, World Health Organization, Geneva

Dr T. Fujikura, Scientist, Veterinary Public Health, Division of Communicable Diseases, World Health Organization, Geneva (Secretary)

Dr F.-X. Meslin, Chief, Veterinary Public Health, Division of Communicable Diseases, World Health Organization, Geneva

Dr K. Stöhr, Associate Professional Officer, Veterinary Public Health, Division of Communicable Diseases, World Health Organization, Geneva

ANNEX II

CASE DEFINITION OF LYME BORRELIOSIS FOR SURVEILLANCE
AND REPORTING SYSTEMS IN THE UNITED STATES OF AMERICA

Lyme disease is a systemic, tick-borne disease with protean manifestations, including dermatologic, rheumatologic, neurologic, and cardiac abnormalities. The best clinical marker for the disease is the initial skin lesion, erythema migrans (EM), that occurs in 60% to 80% of patients.

A case of Lyme disease is defined as follows:

1. A person with erythema migrans; or
2. A person with at least one late manifestation and laboratory confirmation of infection.

NOTE: It should be emphasized that this is an epidemiologic case definition intended for surveillance purposes only.

General clinical epidemiologic definitions:**1. Erythema migrans (EM):**

For purposes of surveillance, EM is a skin lesion that typically begins as a red macule or papule and expands over a period of days or weeks to form a large round lesion, often with partial central clearing. A solitary lesion must reach at least 5 cm in size. Secondary lesions may also occur. Annular erythematous lesions occurring within several hours of a tick bite represent hypersensitivity reactions and do not qualify as EM. In most patients, the expanding EM lesion is accompanied by other acute symptoms, particularly fatigue, fever, headache, mild stiff neck, arthralgias, or myalgias. 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:

These include any of the following when an alternate explanation is not found.

a. 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 as criteria for diagnosis include chronic progressive arthritis not preceded by brief attacks and chronic symmetrical polyarthritis. Additionally, arthralgias, myalgias, or fibromyalgia syndromes alone are not accepted as criteria for musculoskeletal involvement.

b. Nervous system:

Lymphocytic meningitis, cranial neuritis, particularly facial palsy (may be bilateral), radiculoneuropathy or rarely, encephalomyelitis alone or combination. Encephalomyelitis must be confirmed by showing antibody production against *B. burgdorferi* in the cerebrospinal fluid (CSF), demonstrated by a higher titer of antibody

in CSF than in serum. Headache, fatigue, paresthesias, or mild stiff neck alone are not accepted as criteria for neurologic involvement.

c. **Cardiovascular system:**

Acute onset, high grade (2nd 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 accepted as criteria for cardiovascular involvement.

3. **Exposure:**

Exposure is defined as having been in wooded, brushy, or grassy areas (potential tick habitats) in an endemic county no more than 30 days prior to the onset of EM. A history of tick bite is not required.

4. **Endemic county:**

An endemic county is one in which at least 2 definite cases have been previously acquired or a county in which a tick vector has been shown to be infected with *B. burgdorferi*.

5. **Laboratory confirmation:**

Laboratory confirmation of infection with *B. burgdorferi* is established when a laboratory isolates the spirochete from tissue or body fluid, detects diagnostic levels of IgM or IgG antibodies to the spirochete in serum or CSF, or detects a significant change in antibody levels in paired acute and convalescent serum samples. States may determine the criteria for laboratory confirmation and diagnostic levels of antibody. Syphilis and other known causes of biologic false positive serologic test results should be excluded, as appropriate, when laboratory confirmation has been based on serologic testing alone.

ANNEX III

LYME DISEASE CASE REPORT FORM

Patient's last name _____ First name _____ Tele.No. (____) _____

Address _____ City _____

Detach before sending to CDC

State _____ County _____ Zip _____

Age (yrs.) _____ Sex M F Unspec. Race Amer. Indian/Eskimo Asian/Pacific Isl. Black White Unknown Ethnicity Hispanic Non Hisp. Unknown

SYMPTOMS AND SIGNS OF CURRENT EPISODE (PLEASE MARK EACH QUESTION):

DERMATOLOGIC:

Erythema migrans (physician diagnosed EM at least 5 cm in diameter)? [Y] [N] [?]

RHEUMATOLOGIC:

Arthritis characterized by brief attacks of joint swelling? [Y] [N] [?]

NEUROLOGIC:

Bell's palsy or other cranial neuritis? [Y] [N] [?]

Radiculoneuropathy? [Y] [N] [?]

Lymphocytic meningitis? [Y] [N] [?]

Encephalitis/Encephalomyelitis? [Y] [N] [?]

CSF tested for antibodies to B. burgdorferi? [Y] [N] [?]

Antibody to B. burgdorferi higher in CSF than serum? [Y] [N] [?]

CARDIOLOGIC:

2nd or 3rd degree atrioventricular block? [Y] [N] [?]

Other clinical: _____

Date of onset of first symptoms: / /
mo dy yr

Date of diagnosis: / /
mo dy yr

Date of report to health agency / /
mo dy yr

OTHER HISTORY

Was the patient hospitalized for the current episode? [Y] [N] [?]

Name of antibiotic(s) used this episode? _____ Use in days _____

Was the patient pregnant at the time of illness? [Y] [N] [?]

Where was the patient most likely exposed? County _____ State _____

LABORATORY RESULTS

Serologic test results: Positive Negative Equivocal Not done/Unknown
Culture results:
Other (specify)

Physician's name _____ Person completing form _____
(if not the same)

Address _____ Address _____

Telephone Number (____) _____ Telephone Number (____) _____

FOR INTERNAL USE ONLY

State ID No.

CDC ID No.

Date Reported to CDC / /
mo dy yr