Borrelioses West '89

October 13-14, 1989
Oakland, California

Hyatt Regency Oakland
1001 Broadway,
Oakland, CA 94607

Sponsored by
The Lyme Borreliosis Foundation

Co-Chairmen:
Robert S. Lane, Ph.D.
Associate Professor of Entomology
University of California at Berkeley

Paul E. Lavoie, M.D., FACP
Associate Clinical Professor of Medicine
University of California at San Francisco

CONFERENCE FEE

The registration fee is $150 per attendee.

CME CREDITS

CME credits will be available through Pacific Presbyterian Medical Center.

HOTEL RESERVATIONS

The Hyatt Regency Oakland, built in 1983, offers all modern conveniences. Located in the heart of Oakland, it is connected to the Oakland Convention Center, and it is 10 minutes from Oakland Airport, 30 minutes from the San Francisco Airport, and 15 minutes from San Francisco on BART public transportation.

To make your hotel reservation, please contact: Gail Weiss, Conference Coordinator. Telephone 1-800-336-0033
Discount flight arrangements are also available.

QUESTIONS?

Please call 203-381-4092

Borrelioses West '89 October 13-14, 1989 Oakland, California

#4.
10/13-14/89

San Fran/Loma Prieta Earthquake
10-17-89.
Strongest Earthquake since 1906!
63 deaths, 3,800 injuries
#6 billion in property damage.
6.9 in magnitude.
Karen, Tom & Jamie were in a car in the middle of it - Bridges collapsed, Road pavement broke, fire broke out everywhere. This was also known as the World Series Earthquake!

Friday, October 13, 1989
Afternoon Session

1300: Opening Remarks
Robert S. Lane, Ph.D.

1310: Lyme Borreliosis.
A Relapsing Fever-Like Illness?
Willy Burgdorfer, Ph.D.,
Scientist Emeritus,
Rocky Mountain Laboratory, Hamilton, MT

1340: Centers for Disease Control: Role in Prevention and Control of the Borrelioses.
Joseph Piesman, Ph.D.
C.D.C., Fort Collins, CO

1400: Lyme Borreliosis in California:
A Descriptive Study.
Robert Murray, Ph.D., Epidemiologist,
California Department of Health Services,
Berkeley, CA

1420: Northern California Lyme Disease Study.
Robert Werra, M.D.
Family Practitioner, Ukiah, CA

1440: Lyme Borreliosis: Identification of Environmental Risk Factors.
James Clover, B.S.
Vector Control Specialist, CA
Department of Health Services,
Santa Rosa, CA

1500: Coffee

1530: Veterinary Aspects of Lyme Borreliosis.
John Madigan, D.V.M.
Associate Professor of Veterinary Medicine,
University of California at Davis

1600: Molecular Biology of *Borrelia burgdorferi*.
Tom Schwann, Ph.D., Scientist
Rocky Mountain Laboratory, Hamilton, MT

1610: *Borrelia burgdorferi* Isolates from Ticks and Wildlife.
John Anderson, Ph.D.
Director, Connecticut Agricultural Experiment Station

1630: Epizootiology of Lyme Borreliosis in California.
Robert S. Lane, Ph.D.

1700: Panel

1730: Lyme Borreliosis Foundation:
Purpose and Direction.
Karen Forschner, Founder.

Saturday, October 14, 1989
Morning Session

0800: Opening Remarks.
Paul E. Lavoie, M.D., Moderator

0815: Comparative Immunobiology of the Spirochetes.
James Miller, Ph.D.
Professor of Microbiology
University of California School of Medicine at Los Angeles

0845: Experimental Pathogenesis of *Borrelia burgdorferi*.
Michael Lovett, Ph.D.
Associate Professor of Medicine,
University of California School of Medicine at Los Angeles

0915: Laboratory Diagnosis of Lyme Borreliosis.
David A. Lennette, Ph.D.
Evelyne Lennette, Ph.D.
VIROLAB, Inc., Berkeley, CA

0935: Pathology and Dermatology of Lyme Borreliosis.
Paul Duray, M.D.
Pathologist, Fox Chase Cancer Center,
Philadelphia, PA

1005: Coffee

1035: *Borrelia burgdorferi* Serology in Multiple Sclerosis.
Julia Rawlings, M.S.
Microbiologist, Texas Department of Health, Austin, TX

1055: Neuropsychiatric Manifestations of Lyme Borreliosis.
Andrew Pachner, M.D.
Associate Professor of Medicine,
Georgetown University, Washington, DC

1125: Ophthalmologic Findings in Lyme Borreliosis.
Allan Flach, M.D., PharmD.
Associate Professor of Ophthalmology,
University of California at San Francisco

1155: Lunch

Saturday, October 14, 1989
Afternoon Session

1325: Opening Remarks
Willy Burgdorfer, Ph.D., Moderator

1330: The Western Chronic Borrelioses:
Preliminary Observations
Paul E. Lavoie, M.D.

1400: Treatment of Late Lyme Borreliosis:
Options and Guidelines.
Joseph Burrascano, M.D.
Internist, East Hampton, NY

1430: Entomologic and Microbiologic Observations of *Borrelia burgdorferi* in Missouri.
Dorothy J. Feir, Ph.D.
Professor of Biology
St. Louis University, MO

1455: Early Clinical Observation of Lyme Borreliosis in Missouri.
Edwin P. Masters, M.D.
Family Practitioner, Cape Girardeau, MO

incl. Preg. & Lyme

1525: Coffee

1600: Chronic Lyme Borreliosis:
A Case Report with Sequential Urinary Antigen Measurements.
Valerie Novak, M.D.
Internist, Claremont College,
Claremont, CA

1620: Failure of Published Antibiotic Regimens in Chronic Lyme Borreliosis.
Paul E. Lavoie, M.D.

1650: Panel

Lyme Borreliosis
Foundation, Inc.

National Headquarters
P.O. Box 462
Tolland, CT 06084

(203) 871-2900

Dear Dr. [illegible]:

Critical advances have been made in the diagnosis and treatment of Lyme disease. To bring you up to date on the status of this debilitating illness that now threatens 43 of the 50 states, The Lyme Borreliosis Foundation is sponsoring a conference on October 13-14 in Oakland, California. We invite you to attend.

A panel of twenty-one lecturers, many of whom are distinguished clinical investigators, will be assembled for this one and one-half day conference to discuss the difficulties of diagnosis, the clinical manifestations, and recommended treatment at various stages of the disease. The Conference will enable you to put the latest methodologies to work in your practice.

Please make your reservation today. Attendance is limited to the first 250 registrants. Just fill out the enclosed registration form and enclose it with your check for $150 in the reply envelope. We'll see you in Oakland.

Sincerely yours,

Robert S. Lane

Robert S. Lane, Ph.D.
Co-Chairman

P E Lavoie

Paul E. Lavoie, M.D.
Co-Chairman

P.S. CME credits will be available.

Notes from Borrelioses West '89, Lyme Borreliosis Foundation Conference, October 13-14 by Phyllis Mervine, Coordinator Lyme Disease Clinic, Mendocino Community Hospital, Ukiah, CA tel. 707-463-4674

Opening Remarks. Robert S. Lane, Ph.D, Entomologist, UC Berkeley
5000 - 15,000 estimated new infections each year in US
50,000 in Austria (Staneck)

Lyme Borreliosis. A Relapsing Fever-like illness? Willy Burgdorfer, Ph.D, Scientist Emeritus, Rocky Mtn. Lab., Hamilton, MT.

Estimated erythema migrans in 60%. Relapsing fever - spirochetes are detectable in blood of febrile pts. Study with R. Lane showed 50% Cal. deer infected. Infection peaks on days 11-13 and 17-19, etc. Alternate high and low concentration of spirochetes. Preferred host peromyscus leucopis (white foot mouse). Their experiments were done with mice raised by Benach and Basil with spirochetes from Shelter Is., NY. Procedure: 10^7 spirochetes were injected into each mouse, then uninfected ticks were put on mice. They followed 6 mice which had spirochetemias for 55 days. The % of infected ticks which dropped off varied between 0-100%. Some mice transferred spirochetes much more than others. One mouse infected nearly all the ticks almost all the time. In some mice spirochetes may be present in concentrations too low to detect, and too low to infect the ticks.

Relapsing fever - Borrelia hermsii. 3 - 7 febrile attacks with several days between each (days 4, 11, 19). Mice injected with cultured spirochetes had NO negative episodes. Why? Spirochetes undergo one or more antigenic variations, eluding immune system. Tom Schwann (see below) has identified several specific proteins which play a role in antigenic change. (reported in J Inf Diseases) Borrelia burgdorferi may reside in skin.

Why are the different mice so different? Perhaps immune efficiency and/or size of innoculum. Schwann compared antigenic shift in spirochetes at the beginning and end of period. Protein profile looked similar but reacted differently. A. Pachner (see below) pointed out that we use less than an ideal medium to culture. Bettina in Munich has improved the culture medium.

CDC: Role in Prevention and Control of the Borrelioses. Joe Piesman, PhD, CDC, Fort Collins, Co

During July/August (Lyme disease season) 20% of their calls are on LD. Many on AIDS. People working on LD - Don Quan, LD serology, Bacterial Zoonoses Division. Lyme Section of Molecular Biology Branch. LD Vector Section of Medical Entomology-Ecology Branch. Number of cases (Medical epidemiology figures) from 87 and/or 88: WA 17, OR 27, CA 182, ID 1, NY 3430, CT 577, MN 161, NJ 807, RI 195. LD accounts for >1/2 all vector borne dz in US. Total cases 1987 2368, 1988 4572.

They studied endemic areas to see how many Ixodes ticks were in different types of habitat.

HAB	# LARVAE	#NYMPHS
Lawn	9	24
Ornamental	30	28
Ecotone	43	45
Woods	93	71

Most larvae are in the woods, least in lawns. Rate of infection higher in woods.

Time nymphs fed related to infection of host:

24 hours	7%
48 hours	36%
>72 hours	93%

Different types of Ixodid ticks and their habitats:
Ix. persulcatus - Eurasia
Ix. ricinus - Europe
Ix. scapularis - South US
Ix. dammini - NE US
Ix pacificus - W US
Ix. dentatus - N America

Lyme Borreliosis in California: A Descriptive Study. Robert Murray, PhD, Epidemiologist, Cal Dept of Health Services, Berkeley, CA

Hopes that by the end of the year Health Dept will accept specimens for testing (ELISA). Current standard: physician-diagnosed erythema migrans with exposure in area where Ix pacificus is known to exist, no more than 30 days before rash, OR involvement of at least one organ system and positive test or isolation of Bb from clinical specimen. Of 1845 cases 1983-87, 442 (24%) met case definition.
43% positive serology
50% EM
51% recalled tick bite
Number of cases by County,1983-87: Humbolt 108, Mendocino 123, Sonoma 21, Marin 30.
Median age at diagnosis 37, compare other studies ages 5-9.
Month of onset of EM: slight summer peak, especially June, with other high counts in March (nymphal stage), May, July, August.
A. Pachner: How may seronegative of different racial groups?
Ans. Using anticomplement IFA at Virolab, 95% Caucasian, 3% Hispanic.
(Unanswered: what % of sample was Cauc, Hisp?)

Northern Cal Lyme Disease Study. Robert Werra, MD, Family Practitioner, Ukiah, CA

200 cases per 100,000 population in Mendocino County. Same as Long Island where tick infection rate is 30%.
R. Lane: tick infection rate 1-2% except one area tested along Russian River in Sonoma County where rate was 5-6%.

Lyme Borreliosis: Identification of Environmental Risk Factors. James Clover, BS, Vector Control Specialist, Cal Dept of Health Services, Santa Rosa, CA.

R. Lane: In early summer 1/2 ticks biting humans which were sent in were Dermacentor.
Map slide with different colored dots: positive ticks found in Cal.
Only counties in Cal not reporting Ixodes ticks: Kings, Mono, Modoc, Alpine, San Joaquin.
Ixodes pacificus ticks require high humidity. They can't stand direct afternoon sun and are found more frequently on north and east facing slopes. Adult, nymph and larvae are found in different habitats. Closer to coast not so much shade is necessary. They depend not only on humidity but presence of proper hosts. The average level for questing behavior is 55 cm above the ground. In area with complete canopy, heavy shade, tick population lasts longer into summer. At on shady site JC found many larvae but no females. Has found ticks at 6500 feet. Ticks can wait for host 1 - 2 months.

Veterinary Aspects of Lyme Borreliosis. John Madigan, DVM, Assoc. Prof of Vet Medicine, UC Davis.

Several yrs ago studied prevalence of Bb in dogs in northern Cal, Mendo and Humbolt Counties. 434 dogs tested IFA ATTC Bb antigen strain. Positive >1:64 Where no human Lyme dz was reported, dogs were negative. Average 26% dogs positive, range from 7% in north to 48% in s. Humbolt. Ukiah of 86 dogs #24 were pos. Willits 73 dogs #28 positive. Of positive dogs 33% were lame, 24% had no clinical signs.
No leptospirosis cross reaction, IFA X reactions to B hermsii, B corriaceae. Are there others?
Sx in dogs: arthritis, kidney dz, heart dz, neurologic. Sudden lameness, short duration, multiple episodes, sometimes fever. Oct. 89 report includes anorexia, weight loss, lameness. Study from Conn.: lameness 91%, fever 45%, anorexia 43%. Titre does not correlate with clinical dz.
JC Frank JAVMA June 89.
Seropositive, asymptomatic dogs sometimes develop later dz. Two owners in Willits came down with Bells palsy and then their dogs got it too. (Tried to line them up for a group photo). Not much work on cats because they scratch when you try to take their blood. Rx based on what is being used in humans.

Molecular Biology of *Borrelia burgdorferi* . Tom Schwann, PhD, Scientist, Rocky Mountain Lab, Hamilton, MT

Attempting to improve Dx, understand pathenogenesis, develop vaccine.
Serial passage of Bb - loss of infectivity as result of *in vitro* cultivation in artificial medium, especially two particular plasmids were lost which enable spirochete to establish infection in host. Also noted between the 10 -15th passage (same as period they lose ablility to infect) is loss of outer surface proteins.

Work on detecting the target organism in infected individual, including detecting single spirochetes.
WB comment: We never have the isolate the individual was infected with when we test his/her serum.
?What about using Western Blot to confirm? They get very different results when tested against a strain which has been passed through several passages.
Western Blot - what is positive? Lack of standardization.

***Borrelia burgdorferi* Isolates from Ticks and Wildlife.** John Anderson, PhD, Director, Conn. Ag. Experiment Station, New Haven, CT

Slide of tick mouth parts - excellent
Six species of Ixodes tick. Ix. dentatus rarely feeds on humans. Habitat eastern 1/2 of US overlaps other tick areas.
Larva and nymph feed 3-4 days
Adult female feed 9-11 days.
Study of white footed mice live caught in diff states:

State	% infected mice	% infection rate of ticks
CT	86	<35
RI	78	12
NY	65	<61
WI	88	?

Areas where fewer ticks are infected either have no reptiles or if they do, ticks don't feed on them.
Our US isolates have more differences among each other than do European isolates. Different variants of Bb, not known if or how this related to human dz.

In East 8 of 11 mice are infected with Babesioti microti, 10 of 11 with Borrelia burgdorferi.

J Clinical Microbiology (date?) Antigenic profiles of spirochetes. Effects of variants of humans not known.

Epizootiology of Lyme Borreliosis in California. Robert S. Lane

He is looking at the reservoir mechanism, i.e. how Bb is perpetuated and distributed, and at ecological and epidemiological factors associated with human risk. Feels we are dealing with a single species of spirochete with variants.
Pacific Coast tick - vector of Rocky Mt. spotted fever (0.4 - 0.5% infected) many not infected with Bb. A sentinel animal -black tail jackrabbit, 90% infected in parts of Mendocino county.
Lizards are by far the preferred hosts of larval and nymphal ticks.
Zooprophylaxis - a term coined by Spielman to refer to the phenomenon of attachment of vector ticks to a reservoir-incompetent host (in this case, lizards). They have never been able to recover spirochetes from infected lizards.
Important to remove tick mouthparts from bite site to prevent possible secondary infections.

Panel Discussion

Whether or not tick gets infected depends on certain concentration of pathogen in host animal.
Whether or not infected tick transmits disease - speculations: antigenic variation of spirochete? Can organism be in a non-infective state? WB: believes spirochete must be in a pathogenic state. ONE spirochete would be enough (as *treponema pallidum*). Duration of attachment extremely important. JA: Do ticks appear flat? In Connecticut they are weighing ticks to see how well fed they are. Nymphs don't start sucking blood for 10 hours (*on body or after attachment?)* Dr. Bernhard Berger had a pt with EM after 8 hrs. Contradicts above. WB: Spirochete may be injected with the saliva. With Colorado tick virus, if you're bitten, you get it. There is a time consideration with Rocky Mt spotted fever. JC: Inappropriate removal of tick (i.e. squeezing body, using match, alcohol, etc.) enhances RISK. Tick may regurgitate. BL: No one knows how long it takes for ticks to transmit dz. They are setting up an experiment now. Eastern ticks 5% have generalized infection (including salivary glands), 95% only the hind gut is infected. Figures for Western ticks are unknown.
WB: New tick-removing gadget developed in Sweden called "The Tick Solution." It works. Cost ~$10.
WB: Infection is possible through unabraded skin. True also of relapsing fever. Multiple infections possible - no immunity. JP: minimum inoculum - 10^3 spirochetes were injected intraperitoneally into hamsters. The requirement for intradermal infection may be lower.
Ecology RM: No evidence dz is spreading (*in Cal*)
JA: East US number of ticks is increasing. In early part of the century, I*xodes dammini* in Pennsylvania was very rare, up until 1960 and even 1970 Spielman doesn't mention them. Now there are thousands, 80% infected.
Vector Control
JA: Ticks have no good natural enemies. Birds will eat them. A predatory wasp was introduced and established on island in Massachusetts. The wasp lays eggs in engorged ticks. They destroyed 20 - 30% of Ix. ticks but there are still plenty left.
TS: There is a certain bird (*ospecter?*) that picks ticks from elephants, rhinos.
JP: Up to 40% of nymphal ticks on above mentioned island were parasitized, but there were just as many adult ticks on deer as on a neighboring island where there were no wasps.
JA: In June Connecticut robins carry av. 20 - 30 ticks.
WB: *Ixodes ricinus* feeds predominantly on birds.

Comparative Immunobiology of the Spirochete. Michael Lovett, PhD, Associate Professor of Medicine, UCLA School of Medicine

Human Spirochetoses: Syphilis -How *Treponema pallidum* produces disease. Difficult to cultivate, fragile. Can only be grown *in vivo* (rabbit testes). Chancres appear weeks after infection and last for weeks or longer. There is an active host immune response (first symptom). Then this disappears and second stage appears. Oranism is not phased by the host immune response. Eventually organism is forced into a latent phase.

1. dissemination
2. chronicity (evasion of host immune response)
3. recrudescence

If you have specific antibodies and mix antibodies with the bacteria, they bind. However with Treponema p. you must kill, wash, remove outer membrane of spirochete before they become immunoreactive (FTA-ADS fluorescence test). Living Tp resist binding, you have to add complement for 8 - 16 hours under ideal i*n vitro* conditions to kill them, before antibodies can bind.

Speculations on antigenic inertness, and how they avoid being killed:

1. coat with host molecules (wolf in sheep's clothing idea)
2. innate Tp cell architecture (unique membrane - no precedence for this idea)

Freeze fracture electron microscopy - can unzip 2 layers of cell membrane so you can see what's inside. Tp has two coats, inner and outer. There are rare outer membrane proteins.

E coli	6000 - 10,000 outer membrane proteins
T pal	70
Aurantia	500
Bb	1800 Using B 31 lab strain

Longer *in vitro* cultivation raises surface proteins. Maybe *Borrelia burgdorferi in vivo* has rare outer membrane protein.

Where leptospirosis attach to cells is a plaque of adherence at binding site. Dr. Bartholt at Yale provides them with synovia from rats with Bb arthritis.

Experimental Pathogenesis of BKorrelia burgdorferei. James Miller, PhD, Professor of Microbiology, UCLA School of Medicine

Epithelial attachment (direct bloodstream intervasion or via lymphocytes) >>
Vascular lumen (resistance) >>
Endothelial attachment (intervasion of barrier) >>
Tissue invasion (latency, evasion of antibody-mediated lysis)

1. attachment - 1974 demonstration

Lovett - invasion via intercellular junctions

2. mediated by 3 protein ligands (polypeptides)

Important initial step in establishing a colony. They "march" right through. Cells are not changed. Other non-pathogenic spirochetes do not show this characteristic. Where do they establish themselves and what are they doing in latency?

Slide of *T pallidum* inside a monolayer cell, within the cytoplasm.

In 1/3 of latent pts something upsets the balance in favor of the organism..

Immune response is directed against 22 polypeptides. However there is a waning of antibody, eventually it reacts only to 10 polypeptides.

Virulent strains of Leptospira attach more, better, invade more. Avirulent strains attach but not to same extent. Attachment can be blocked with monoclonal XXX? *(basis for vaccine work?)*

Intervasion (penetration of monolayers) does occur.

Both virulent and avirulent strains occur in junctions between cells.

Take up intracellular residence. Membrane bound.

It is unknown whether they are being taken up as a mechanism for survival.

However, B 31 avirulent aboratory strain of Bb does NOT get into intercellular junctions. Once Bb gets into organs and tissues how does it survive? Phenomenon of attachment may be a prelude to entry into a cell.

Laboratory Diagnosis of Lyme Borreliosis. David Lennette, PhD, VIROLAB, Inc., Berkeley, CA

1. Direct detection by immunofluorescent staining. Organisms found most frequently in skin (EM), rarely in brain or synovia
2. Culture. Skin lesion biopsy most efficient. Less effective: blood plasma, CSF, synovial fluid.
3. Serologic assays.

IFA - indirect immunofluorescence. Not as specific
ELISA - enzyme-linked immunosorbent assays
ACIF - anti-complement immunofluorescence (used by Virolab since '85, sensitive amd specific)
WB - Western Blot
Problems:
Lack of absolute standards and characterized reference panels. Need to set cut-off for IFA and ELISA (grades of variation, especially with ELISA)
Delay in seroconversion. First 4 - 6 weeks negative often changes subsequently.
Cross-reactions, known and unknown.

Pathology and Dermatology of Lyme Borreliosis. Paul Duray, MD, Pathologist, Fox Chase Cancer Center, Philadelphia, PA

T pallidum - many more in a lesion than Bb. Looks quite different on slide. Bb rare organisms.
Borrelia plaque infiltrate mimics lupus profundus.
Swollen liver - changes which look like viral hepatitis.
Myocarditis
Lichen plantis-like eruption of skin (Bb)
Lymphoma
Granuloma annulari
Folliculitis
Myocitis
Myelin loss
Proliferation of synovia, laying down of fibrin
Obliteration of small vessels, plasma cells situated around capillaries
Localized morphea
Scleroderma
Vitiligo, depigmentation (immune phenomenon)

***Borrelia burgdorferi* Serology in Multiple Sclerosis.** Julia Rawlings, MS, Microbiologist, Texas Dept of Health, Austin, TX

Isolated spirochetes from pts, 1/2 never had titres.

1979 MS first described accompanied by demyelinating myopathy, progressive, relapsing.
Rate of MS 60 per 100,000 population, mostly in northern climates, especially in first 15 years of life. Elevated antibodies to measles in 40%.
Gabriel Steiner postulated that it was caused by different spirochetal dz which he named spirocheta myelophthora, the myelin sheath-destroying spirochete.
MS is associated with sinus infections and naso-pharyngeal infection. JR wanted to prove that some cases of MS are caused by Bb.
Of 81 MS pts, 17% were positive for Bb.
Of 180 matched controls, 6.7% were positive for Bb.
3.3 X risk
By IFA 93 MS pts 14% positive
79 family members of the pts 5% positive
Of 89 MS pts 20 (23%) had elevated antibodies to rubeola
Only 5% of the controls had elevated antibodies to rubeola
Antibodies could be higher during exacerbations.

Neuropsychiatric Manifestations of Lyme Borreliosis. Andrew Pachner, MD, Assoc. Prof. of Medicine, Georgetown University, Washington, DC

Borreliosis differs from syphilis in that there is a paucity of Bb organisms compared to Tp. Mouse studies show that the organism can get to the brain very early in the infection. Commonly we do not see psychiatric manifestations, however many get meningitis which may be minimal and may be missed.
Headache and stiff neck 64%
Fever and chills 56%
Malaise, fatigue, lethargy 80%
Symptoms of encephalitis:
Difficulty in concentrating, poor memory, emotional lability, clumsiness, sleep disorders, irritability caused by diffuse inflammation of the nervous system.
Painful radiculitis may be confused with disk disease (usually cervical).
Patterns may be related to individual genetics or to different strains of Bb.
Early dz does not look like MS to a neurologist, however later it does.
Difference between *in vitro* and *in vivo* strains: plasmids of Bb change after they are injected into animals.
Behavioral changes - depression
anorexia nervosa
Memory difficulty
Subacute encephalitis - confusion
agitation
disorientation

CNS symptoms rare
Cranial nerve palsies
para and tetraspastic pareses
flaccid pareses
sensibility disorders
bladder
ataxia, etc.
AP recommends lumbar puncture

CSF pleocytosis occurs later in illness. Elevated white cell count. EEG usually will be abnormal. Neuropsychological testing. MRI works in 5% in showing lesions, better for specific abnormality, not good for diffuse lesions.
Not comfortable with seronegative Lyme dz. Runs 6 negative controls on each ELISA plate. Does Western blot on all positives but does not consider it the Gold Standard.
Diagnostic Criteria:
CNS abnormalities without another documented cause
Antibody
Response to antibiotic therapy.
Treatment:
IV only for brain involvement except for Bell's palsy with normal lumbar puncture, otherwize 1 month doxycycline.
If pts don't respond he considers it a "self-perpetuating immune response."

Ophthalmologic Findings in Lyme Borreliosis. Allan Flach, MD, PharmD, Assoc. Prof. of Ophthalmology, UCSF

Signs:
Scleritis -
Bell's palsy
Blepharitis
Episcleritis
Conjunctivitis (11 - 20%)
Panophthalmitis
Anterior uveitis
Symptoms of III and VI nerve involvement:
- Diplopia
- Photophobia (most common)
- Ocular pain
- Decreased vision

Many slides of eye, retina, changes in Bb infection.

The Western Chronic Borrelioses: Preliminary Observations. Paul E. Lavoie, MD

Sun-induced vesiculating rash on arm not described by dermatologists.
Ectopy - heart flutters.
Acneform rash (B hermsii)
B coriaceae infection of humans not previously recognized, however habitats of Ornithodorus coriacius and Ixodes pacificus overlap.
% infection rate of O coriacei:
Larvae 1%
Nymphs 8%
Adults 24%

Relapsing fever - B parkeri and B turiculi as well as B hermsii.

Treatment of Late Lyme Borreliosis: Options and Guidelines. Joseph Burrascano, MD, Internist, East Hampton, NY

Important to choose the right antibiotic. Drugs that work i*n vitro* do not always work *in vivo*.
Amoxicillin - 1st choice
Ceftin - very expensive, GI problems more frequent
Ceftriaxone - expensive, 2 g dose associated with liver problems, gall bladder sludging.
Claftoran - may be better
Probenecid - may lower brain levels of penicillin

Are there other forms of spirochetes (eg. blebs, budding forms) which would resist tx or require different tx? What about dormancy, latency?
Definition of Successful Outcome: does not believe in "post Lyme syndrome" in which symptoms continue but at a lower level.

cured by his standard in less than 60 course of tx
3 of 105 pts on doxycycline (45 days)
0 of 39 pts on tcn
0 of 42 pts on pcn V
15 of 108 pts on amoxicillin (30 day minimum)

Compare Ceftriaxone as sole therapy:
0 of 4 pts treated for 10 days
0 of 15 pts treated for 14 days
0 of 10 pts treated for 21 days
0 of 2 pts treated for 28 days
0 of 8 pts treated for 6 weeks

Duration of therapy is just as important as choice of antibiotic.

Months on amoxicillin/ probenecid	1	2	3	4	5	6
% pts cured	12.5	18	35	36	66	66

After 6 months cure rate levelled off with no more pts any better after 6 months tx than they had been on 5.

Endpoint: If pts still have symptoms they will relapse if you stop antibiotic tx.
Follow all IV treatments with oral to same endpoint.
Individualize Tx
Take very careful histories
Minimum 30 day Tx, average 4 months.
Factors in failure of Tx: multiple tick bites
active synotivis with high ESR
Factors in failure of oral Tx leading to IV: Age > 60
Synovitis with high ESR
Predominantly CNS symptoms
Prior use of steroids

Herxheimer day 4 - 5 with PO Rx
day 1 - 3 with IV Rx

lasts 1 - 2 weeks.
Later onset or longer duration of Herxheimer predicts need for longer Tx. May have to interrupt Rx if Herx. severe.

Many pts experience a monthly (average 4 weeks) cycle of symptoms. Flares may be reflected in IGm peaks. Other infections can cause a flare of LD. Subsequent Lyme exposures are usually more severe. One the interleukin is primed, a much lower dose is required to set it off.
Seronegative conversion rate - 36%
Causes of failure of response:
- non-compliance
- alcohol use
- not enough rest

Beware of allergies to probenecid (sulfur base).
Pts on doxy should protect skin and eyes from sun.
Lab. tests every 4 to 6 weeks while on antibiotics.
Pts advised to eat yogurt or acidophilus daily.
Pts must sign an informed consent to treatment.
Pts advised to take vitamins.
Listen to PT and work together.

Entomologic and Microbiologic Observations of *Borrelia burgdorferi* in Missouri. by Dorothy Feir, PhD, Prof of Biology, St. Louis Univ, MO

Collect animals, collect ticks off animals.
From 2.4 to 2.8% of Ablyoma americanum, the Lone Star tick, are infected with Bb. 1.5% of Dermacenter are infected with Bb.
Study with rabbits wearing little jackets so they couldn't scratch off ticks.
Showed transmission with Lone Star tick, possibility it is a real vector of Lyme dz.
WB: Do the spirochetes survive into the next state when the tick moults? According to tests by WB and JP, spirochetes do not survive in Ixodes scapularis.

Early Clinical Observation of Lyme Borreliosis in Missouri. Edwin P. Masters, MD, Family Practitioner, Cape Girardeau, MO

No Ixodes ticks. Ix scapularis has no spirochetes. However Ablyoma and Dermacenter do..
Size of inoculum may affect speed of reaction in pt. Larger ticks perhaps require shorter transmission time.
Many slides of erythema migrans.
Put add in paper Lyme Researchers Offer $.05 Per Tick People brought in ticks, everything going well until last day, a lady came in with 20,000 ticks. He had to write her a check for $1000.

Lyme Disease in New Jersey. John Druelle, MD, Internist

80% of his and his wife's practice (she is an MD internist also) is LD related.
They get an average of 150(?) LD pts per week.
Reasons for seronegativity:
- lack of antibody production
- immuno-suppressive effect of Bb infection
- curtailment by early and late antibiotic Tx
- use of variety of Bb strains and antigens by different labs.

His own experience is 24% seronegative.
A single negative lab result does not exclude LD.
Immune complex formation: Serologic tests only detect free antibody. If antibody is complexed in active LD this could result in negative serology. Immune complex digests may free sequestered antibody and allow detection.

Dianon Urine Antigen Test: Using 43 pts, all seronegative with 1 - 10 years symptoms, 12 of them previously treated and relapsed. All had positive urine antigen, not a constant rate, and they had to load pts with antibiotics to get peak concentration in urine. With further Tx 38 of the 43 had significant improvement.

Allan MacDonald - Nov. '89 article
- 14 cases of spontaneus abortion or perinatal death
- 10 autopsies showed evidence of Bb in tissue and placentas
- 4 live births with Bb in placentas
- 10 pts with abortions, mothers were negative
- 2 had ECM during pregnancy with TX and "successful" outcome

Study:
Mothers with asymptomatic seronegative Lyme disease ~~have~~ had a higher incidence of spontaneous abortion and malformations of fetus.
Positive moms had no fetal deaths or miscarriages
This argues against mass screenings for LD. Women more at risk would be missed. However urine antigen test might work for a mass tool:
- Specificity of UA test is high
- Sensitivity of UA test is low

Complete or partial remission rate:
- Pen G 57.5% 20,000 U qd X 10 days
- Cefotaxine 87% 3 g q 12 hrs X 10 days (This is a German figure. Either their Bb responds differently or Europeans are not starting with oral tx or ???) US children respond better, nearer 80%. They treat children with IV right away.

Chronic Lyme Borreliosis: A Case Report with Sequential Urinary Antigen Measurements. Valerie Novak, MD, Internist, Claremont College, Claremont, CA

During serum sickness antigen release was highest. Antigen measurement fluctuated between negative, positive and high positive.

Failure of Published Antibiotic Regimens in Chronic Lyme Borreliosis. Paul E. Lavoie, MD

Published treatments were in use before we even knew what caused the disease.
1985 NEJM Successful Parenteral Penicillin Therapy, Allen Steere, 55% responded. Now down to 45%.
Review of the literature
Meningoencephalitis - Durringer and Halperin
1. available antibiotics only effective during microbial reproductive phase (includes Ceftriaxone)
2. microbial killing follows exponential delay rules
3. ?
Observe symptomatic flares while on prolonged antibiotic therapy, and typical cessation of flares if antibiotics are (withheld?). Occasionally there will be elevation of serotitres following flares.
Immune complexes are set down where they are formed.

Panel

What about fever tx for syphilis? Would it work? PL: Malaria Tx for refractory Borreliosis. Used in undiagnosed inflammatory dz. The operating principle is antisepsis. Bb prefer 33 - 34°. Our core temperature is 37°. Spirochetes may reside in the skin. Heat can bring about exacerbation of Sx especially in MS.
JM: Experiments with syphilis. They injected half-shaved rabbits with Trep p and kept them in a cool room. The chancres erupted only on the shaved sides, not on the furry sides. Dangers of fever therapy, among them you can force the microbe into latency, and 2. it blows out aortic aneurisms. You may create more problems.
JD: Treats EM with 6 weeks of amoxicillin/probenecid or Ceftin (expensive), **NOT** TCN or DCN because pts so treated went on to develop advanced dz.
JB: Treats EM 4 to 6 weeks. With constitutional sx treats one month beyond the end of sx. 1 g Amoxicillin tid, or Suprax.
AP: Although 2 weeks is the published "cure," he treats for 1 month. Wants well controlled clinical trials of alternative (including long-term) tx.
Pete Luger uses 3 weeks Amox or doxy, claims no recurrences.
Werra? about unilateral facial swelling
AP: Can't tell the difference between idiopathic Bell's palsy and B p caused by LD. Both kinds resolve without Tx (eventually).
Lyme meningitis can have negative CSF
JM: There are 11 well-defined non-pathogenic host indigenous treponemes, oral, genital, GI. All have X reactive antigens with pathogens. One in the mouth has antigen in common with relapsing fever. Explains low titres - asymptomatic individuals need specific tests. Host response - not everyone responds the same.
JB: Second infection makes people much sicker.
JM: Antigenemia - Is there so much antigen it is binding up antibody and leading to false seronegativity?
AP: Don't accept positive test when there is no clinical evidence. No faith in urine antigen or (*proliferation?*)
JM: Take the spirochetal endoflagella, clone it, sequence it, determine pathogen-unique antigens and create a specific and sensitive test.