



LYME DISEASE and Tick-born Infections

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Lyme Disease

THE POLITICS

There are currently 2 schools of thought on Lyme Disease and the issue is highly political.

IDSA (The International Disease Society of America)

IDSA perspective is that lyme disease is **over diagnosed** that it is **over treated**, that chronic lyme does not exist, and that there is no evidence for repeated treatments or prolonged treatments.

THE POLITICS

ILADS, "The International Lyme and Associated Diseases Society"

Their perspective is that chronic lyme disease does exist, that there is evidence for **repeated treatment** when relapse occurs and that there is evidence for **prolonged treatment**.

Chronic infection does exist and there are plenty of examples which include antibiotic therapy for many years (TB, leprosy) Viral infections (HIV, Hep C)

For really solid studies and evidence that lyme does persist despite a 10 day course of AB's see Dr. E. Maloney's work

- Both have valid arguments and both claim to have research to support.
- Almost impossible to create a valid double blind-placebo controlled study.
- Don't get caught up in the war.

Lyme Disease Defined

- Traditionally, Lyme disease is defined as an infectious illness caused by the spirochete, *Borrelia burgdorferi*
- This is technically correct; clinically the illness is much more than that, especially in the disseminated and chronic forms.
- Furthermore, in the chronic form of Lyme, other factors can take on an ever more significant role; immune dysfunction, opportunistic infections, co-infections, biological toxins, metabolic and hormonal imbalances.

The Bull's Eye

- **Erythema Migrans; Pathognomonic for Borreliosis; 'rash' only occurs in 40-60% of people who are bitten and contract *Borrelia spp.***
- 10% of these rashes are classic erythema migrans ("bull's-eye").

Classic Bull's Eye Rash



Less Classic





- single erythema migrans lacking central clearing



- single erythema migrans with central clearing



A complicated bacterium

Lyme vs. Syphillus

- Borrelia b. has over 1500 gene sequences
- At least 133 of these genes are 'functioning genes'
This gives the organism the ability to survive and change itself.
- In contrast, T.pallidum (Syphillus) has 22 functioning genes.
- Borrelia b. has 21 plasmids; That's 300% (or 3x) more plasmids than any known bacteria! Plasmids are genetic material that allows an organism to have a rapid response system in order to adapt to environmental challenges. This is how bacteria become pathogenic, where they were not pathogenic before. Casjens S et al., *Mol Microbiol* 2000, 35:490-516, Porcella & Schwan, *J Clin Invest* 2001; 107:651-6, Embers et al, *Microbes Infect* 2004; 6:312-318

Lyme Borreliosis (LB)

- There are over 5 subspecies of *Borrelia burgdorferi* (*B. burgdorferi* sensu stricto, *Borrelia garinii*, *Borrelia afielii*, *Borrelia japonica*, and “*Borrelia andersonii*) , **over 40 strains in the US**, and 300 strains worldwide. This diversity is thought to contribute to *Borrelia's* antigenic variability and its various antibiotic resistances.
- <http://www.pasteur.fr/recherche/borrelia/Borreliaspecies.html>
(good site for listing strains and locations that various strains are common)
- Also check out: <http://ijs.sgmjournals.org/content/47/1/1.full.pdf>

How *Borrelia* evades testing

- Stealth Pathology of *Borrelia b.* includes:
 - **Physical seclusion**
 - **Intracellular sites**
 - **Extracellular sites**
 - Phase & antigenic variation
 - Immune suppression
 - Secreted Factors

Where Bb hangs out

- Bb can live in: **Kupffer's cells** (found in liver- filter bacteria and
- other small foreign proteins out of the blood)
 - Brouqui P. et al, "Eukaryotic cells protect *Borrelia* from the action of penicillin and deftriaxone but not from the action of doxycycline and erythromycin" *Antimicrob Agents Chemother* 1996; 40: 1552-1554
- Bb can thrive within **fibroblasts** (cells responsible for making connective tissue)
 - Klempner et al "Invasion of human skin fibroblasts by the Lyme disease spirochete, *Borrelia burgdorferi*", *J Infect Dis* 1993; 167: 1074-81
- Bb can thrive within **lymphocytes and macrophages** (immune cells)
 - Dorward et al, "Invasion and Cytopathic Killing of human lymphocytes by spirochetes causing lyme disease", *Clin Infect Dis* 1997; 25 (Suppl 1): S2-8
- Bb can harbor within **endothelial cells**
 - Ma et al, "Intracellular localization of *Borrelia burgdorferi* within human endothelial cells", *Infect Immun*; 1991; 59: 671-8
- Bb has a proclivity to remain within **synovial cells (joints)**
 - Girschick et al, "Intracellular persistence of *Borrelia burgdorferi* in human synovial cells", *Rheumatol Int* 1996; 16 125-32
- Bb can cross the **placenta**, can cause congenital infection.
- Bb is in **breast milk** and can cause infection through ingestion.

Functional Characteristics of *Bb*

- **Bb selectively binds Oligodendria cells:** These cells are responsible for synthesis and maintenance of myelin: In addition to direct destruction of myelin by bacterium, the host antibodies may attack myelin while targeting *Borrelia* to which myelin is in close contact thus stimulating genuine Multiple Sclerosis
- Garcia Monco JC, etal "Adherence of the Lyme Disease spirochete to glial cells and cells of glial origin" J Infect Dis 1989, 160:497-506

Functional Characteristics of

Bb

- **Often an intracellular organism**

- **Avoids antibody detection and avoids lysis from most beta lactam abx which do not penetrate cells. *Bb* is not present in high numbers in the blood.**
(Penicillins · Cephalosporins · Cephamecins · Carbapenems · Monobactams · Beta-lactamase inhibitors)
- Dorward D, 9th International Conference on Lyme Borreliosis, 1998

- **Microaerophilic**

- **Helical *Bb* will tend to move away from oxygen-rich areas in vivo and reside in fascia, cartilage, epineureum and other oxygen poor areas.**
- Barbour AG et al "Borrelias Strategies for Survival", Science 1987, No 237, pp 403-411

- **Heat Sensitivity**

- **Helical *Bb* may be inactivated and destroyed upon exposure to temperatures of 104 F for 3 hours**
- **Hyperthermia was also used successfully in the treatment of syphilis prior to antibiotics**
- Barbour AG, et al. Science 1987
- From Mercury to Malaria to Penicillin: The History of the Treatment of Syphilis at the Mayo Clinic, 1916-1955

How *Borrelia* evades testing

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 - **Extracellular sites**

- **Phase & antigenic variation**

- Immune suppression

- Secreted Factors

Borrelia morphology

Bb (just likr *H. Pylori*....) currently has a number of recognized life forms

- **Spirochete form**
- **L-form** aka spheroplast (cell wall deficient)
- **cyst form** (also cell wall deficient), which allows dormancy until favorable conditions arise. (this also allows for PCR to miss the organism)
- **Bb can change its morphology to cell wall deficient cysts which are **heat, pressure and oxygen resistant**. Cysts are **resistant to all abx except Tinidazole, metronidazole (Flagyl) and Hydroxychloroquine (plaquonil)**.**
In vitro Cystic *Bb* can readily revert back to helical *Bb*.
- Cystic forms of *Bb* are probably a main reason for treatment resistance and relapse.
- Brorson et al. "Transformation of Cystic Forms of *Bb* to Normal Mobile Spirochetes" *Infection* 1997, No. 25 pp 240-246

Cystic forms are a problem

The effectiveness of antibiotics requires active metabolism by the bacteria, and therefore it is likely that cystic forms of *B. burgdorferi* may be resistant to antibiotic treatment.

These encysted forms may explain why *Borrelia* infection can be temporarily dormant, why a reactivation of the disease may occur when the conditions suit *B. burgdorferi*, and why the infection may relapse after treatment with antibiotics.

Date of Publication: 1997 Source: *Infection*, 25(4):240-246 Authors: (1) Brorson O; (2) Brorson S. Institution: (1) Department of Microbiology, Vestfold Sentralsykehus, Tonsberg

(2) Department of Pathology, Ulleval Hospital, Oslo, Norway”

Epitope Switching

- **Epitope switching:** Bb alternates its outer surface proteins preventing sustained immune recognition and attack.
 - Seller et al, "Immunity to Lyme Disease: Protection, pathology and persistence. Current opinion in Immunology 1996, 8(4): 503-9
- **Slow Division Cycle:** In vitro (in test tube) generation time is 12-36 hours, in vivo (in life) is much longer; perhaps 14-28 days.
 - Chiao JW, Abstract 7th International Conference on Lyme Borreliosis, 1994: Defosse DL et al. "In vitro and in vivo induction of TNF alpha by Bb" Infect Immun 1992; 60: 1109-1113

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Functional Characteristics of *Bb*

- **Bb surrounds itself with hosts own lymphocyte cell membrane:** Avoids detection from host immune system
 - Doward D. et al. Clinical Infect Dis, 1997
- **Bb actively attacks lymphocytes, macrophages, natural killer cells:** Destroys bodies defensive weapons
- This may be why **auto-immunity** happens. Th1 reaction is suppressed while the TH2 response (antibodies) are revved up.
 - Doward D et al. Clinical Infect Dis, 1997

Modes of Transmission

- Various species of ticks carry Bb and other pathogens
- Ticks known to carry Bb include *Ixodes tick spp*, *Ammalyoma americanum* (Western Black Legged tick) and *Dermacentor variabilis* (Wood/Dog ticks)
- Previous studies have demonstrated that a minimum number of hours of attachment needs to take place for transmission to happen based on the time it takes a tick to empty any gut contents into the host. CDC states 24 hrs.
- However there is growing clinical evidence that this may not be the case. Clinically/Anecdotally it may take **4 hours** or less to contract pathogens from a tick bite.
- Pathogens have been located in the salivary apparatus of the tick in addition to the GI and may be expelled on initial bite when **anodyne** and **anticoagulant** materials are released from the mouth.

Differing opinions

- My understanding is that a tick needs to feed for at least 4 hours (some say 24, 36, some 48 (!)) hours before transmitting *Borrelia*. I have read that transmission takes place at the end of the feeding process. Also a tick requires a period (hours?) to settle in before feeding. Thus it can attach for hours without any feeding. In my understanding, the likelihood of transmission of a tick transmitting *Borrelia* if it has not fed is certainly less, but I don't know for sure.

From Umass Tick testing

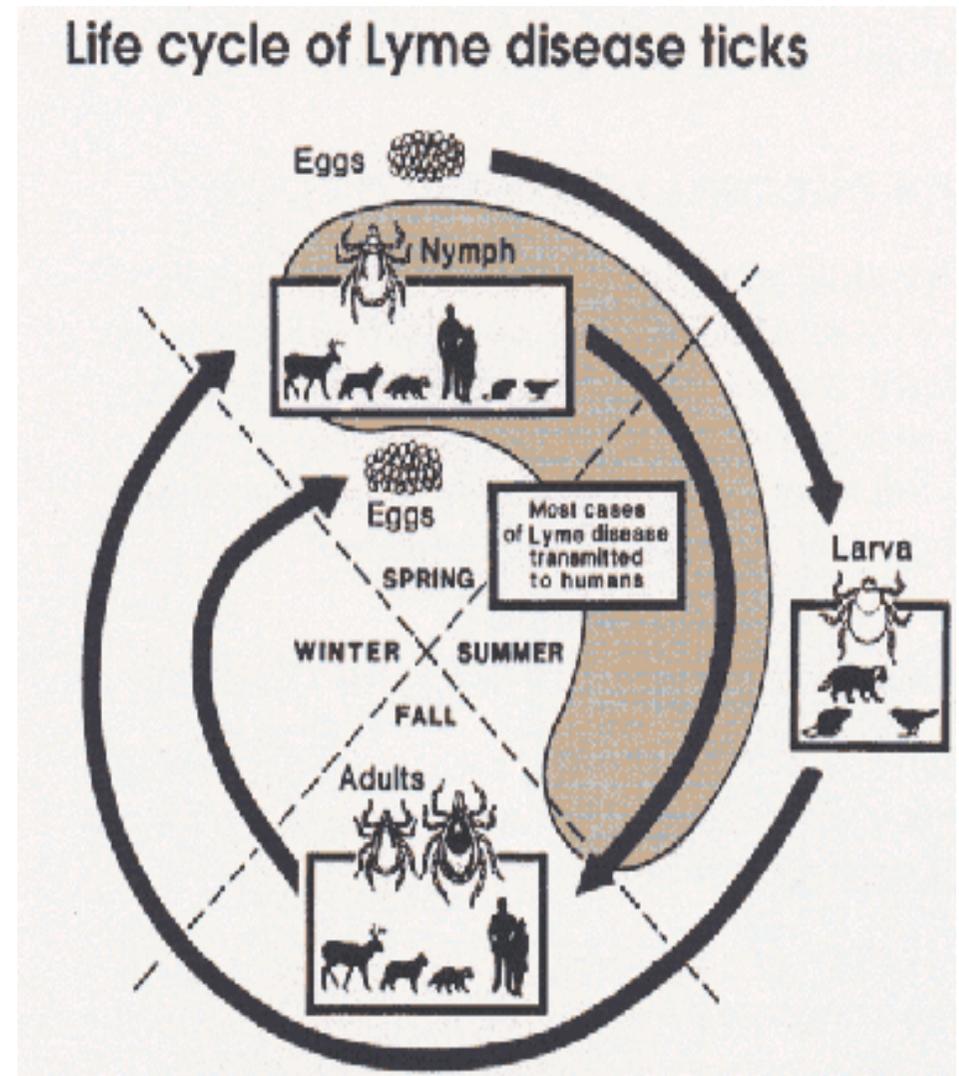
- 2011: 27.5% positive
 - 6% +babesia
 - 3.5%+for Ehrilicia
- 2010: 20.6% positive
- 2009: 26.1% positive
- 2008: 26.7% positive
- 2007: 33.5% positive
- 2006: 21.6 % positive

Speculated Modes of Transmission

- Many "Lyme Literate" physicians observe that Lyme Disease happens in family clusters. What is not known is whether there are common exposures, or other routes of transmission that are yet unidentified/unstudied.
- Another thought is that perhaps the infection is highly prevalent and that certain genotypes predispose to infection developing into disease (HLA typing correlation, genetic detox pathway dysfxn).

Bitten by the Vector

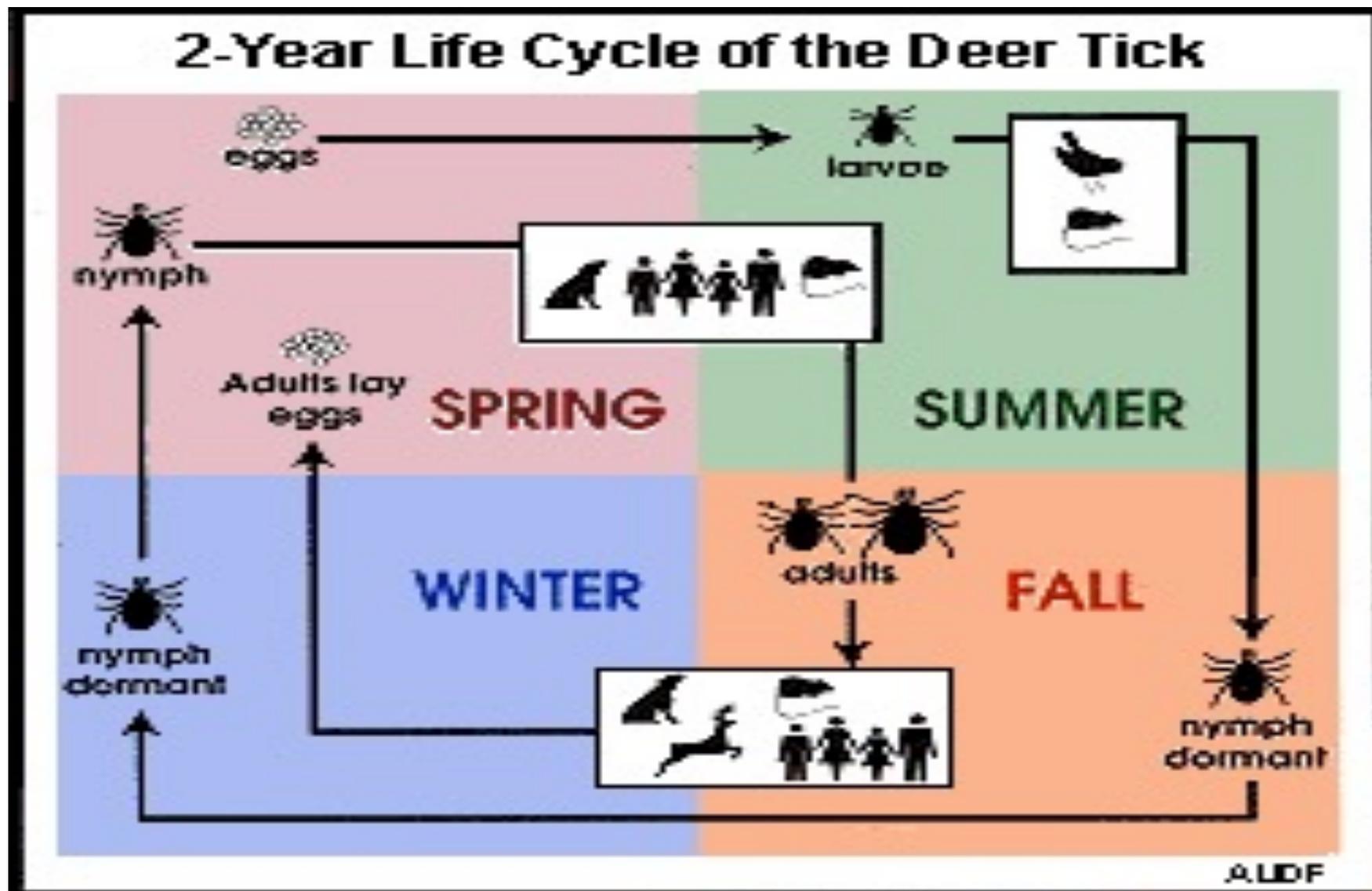
- Only 15%-50% of people with diagnosed Lyme disease recall having been bitten by a tick.
- It is very easy to miss having been bitten by a tick due to the small size in the nymph and larval stages of their lives.



Not all babies are cute.



Life cycle



The Vector

- ***Ixodes scapularis* (Deer Tick)**
- **Deer ticks have a two-year life cycle. That is, it takes two years for one egg-adult-egg generation to evolve. Therefore, deer ticks can be found all year long, including wintertime.**
Male ticks carry Lyme, but they don't attach for as long as females do, therefore they transmit less disease.



1 inch

Blacklegged Tick (*Ixodes scapularis*)



adult female

adult male

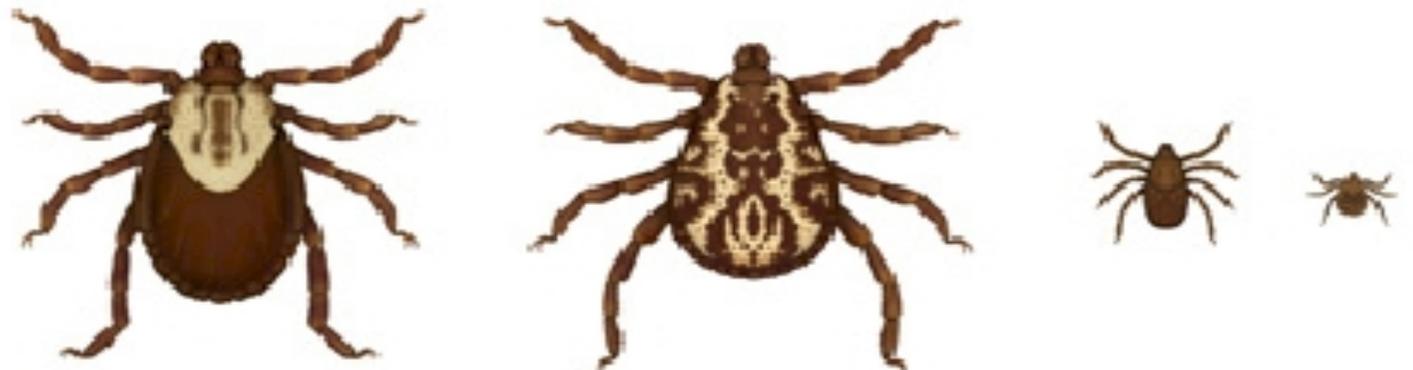
nymph

larva

Lone Star Tick (*Amblyomma americanum*)



Dog Tick (*Dermacentor variabilis*)



2

Prevalence of ticks and Lyme Disease

Lyme disease is **prevalent across the United States**. Ticks do not know geographic boundaries. A patient's county of residence does not accurately reflect their total Lyme disease risk, since people travel, pets travel, and ticks travel. This creates a dynamic situation with many opportunities for exposure for each individual.

Over 40 species of migratory birds have been found to carry the various *spp.* of ticks that carry lyme disease pathogens





How
Under Reporting
occurs

Inclusion criteria for reporting for surveillance:

- erythema migrans OR late stage symptoms
- PLUS
- Isolation of Bb from clinical specimen ie. PCR (high specificity but 20% or less sensitivity unless done on EM lesion) OR
- +ELISA (40-70% sensitivity) PLUS+Western Blot (40-70% sensitivity)

Check it out for your state!

- http://www.cdc.gov/ncidod/dvbid/lyme/ld_rptdLymeCasesbyState.htm

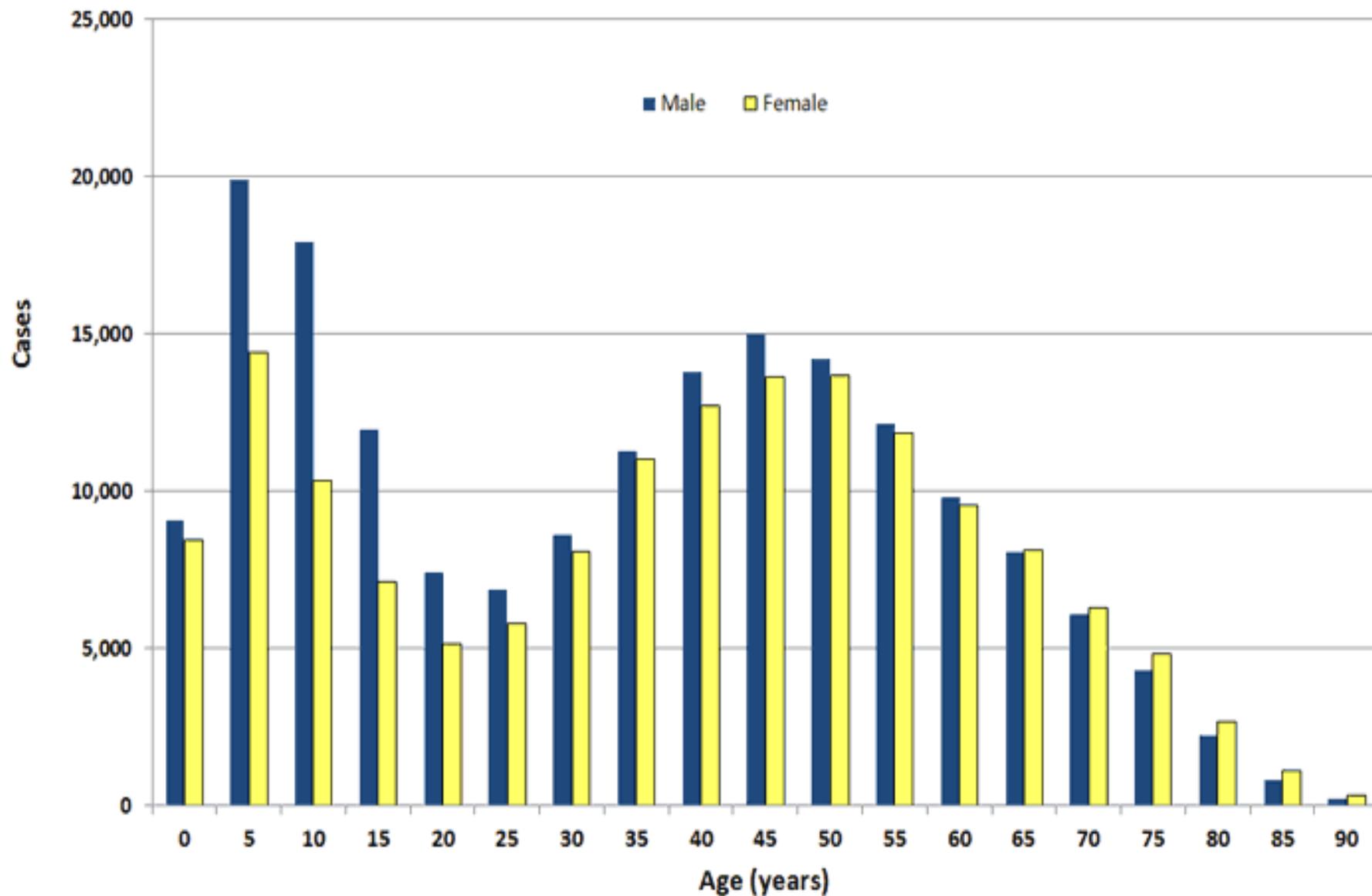
reported from 12 states:

- Connecticut
- Delaware
- Maine
- Maryland
- Massachusetts
- Minnesota
- New Jersey
- New Hampshire
- New York
- Pennsylvania
- Virginia
- Wisconsin
- CDC, 2012

Prevalence & Cost of Lyme Disease in U.S. and Worldwide

- CDC estimates that their disease reporting inclusion criteria in actuality only represents 1/10 to 1/100 of the actual cases that are either undiagnosed or are clinically diagnosed and don't fit the surveillance criteria and as such go unreported.
- The CDC **surveillance** criteria were devised to track a narrow band of cases for epidemiologic change and were **never** set up to be used as diagnostic criteria nor were they meant to define the entire scope of Lyme disease. This is stated in the 3/25/91 NIH report.

5-9 year olds have highest proportion of new cases



PEDIATRIC LYME

- Children between ages 5-9 have the highest proportion of female deer ticks attached for more than 48 hours
- The manifestations of pediatric Lyme disease depends on the age at exposure.
- For kids under three, that had an early tick bite or congenitally acquired Lyme can present with severe hypotonia (poor muscle tone) and developmental delay.

PEDIATRIC LYME

- Behavioral issues, sensory integration disturbances, rage, visual disturbances (which often manifest as a learning disability), delay in both fine and gross motor skills.
- Headaches, joint pain, fatigue, poor temperature regulation and burning in the soles of the feet.

PEDIATRIC TREATMENTS

- Do not use Doxycycline in children under 7 years of age.
- Antibiotics are chosen depending on the severity of Lyme and whether or not there are co-infections.
- Duration of treatment depends on clinical response.
- Rule of thumb: treatment is continued for 2-4 months after all signs and symptoms of Lyme has ceased

Stages of Lyme Disease

- **Early localized:** single EM or rash with no constitutional symptoms. Treat promptly and aggressively referring to ILADS or IDSA guidelines.
- **Early Disseminated disease:** multiple lesions, constitutional symptoms, lymphadenopathy, or any other manifestations of dissemination that are 'mild' and present for less than one year, are not complicated by immune deficiency or prior steroid treatment.
- **Late Disseminated disease:** Symptoms present for more than one year, more severely ill patients, and those with prior significant steroid therapy or impaired immunity secondary to lyme disease or any other reason. REFER to lyme literate physician and co-manage with their direction.

Symptoms in Lyme Disease

- **Every organ & organ system can be affected**
- **Symptoms will migrate and change everyday.**
- **Neuro:** headaches, facial paralysis, seizures, meningitis, stiff neck, burning, tingling or prickly sensations (parathesia), loss of reflexes, or possible increased or normal reflexes with slow return, loss of coordination and equilibrium.
- **Neuropsych:** mood swings, irritability, anxiety, rage ("Lyme Rage"), poor concentration, cognitive loss, memory loss, loss of appetite, mental deterioration, depression, disorientation, insomnia and numerous mood and psychiatric disorders that were not present prior to lyme disease or are extremely exacerbated by lyme disease.
- **Head:** Headache, neck pain, facial pain and paralysis, difficulty chewing, pain in teeth, dry mouth, decreased sense of taste and smell, numb tongue/mouth, peculiar metallic, salty and other tastes in mouth are also common
- **Eyes:** Pain due to inflammation (scleritis, uveitis, optic neuritis), dry eyes, sensitivity to light, ptosis of eyelids, conjunctivitis, blurry or double vision, floaters, difficulty with eye teaming and convergence, swelling around eyes/bags below eyes.

Symptoms in Lyme Disease

- **Ears:** pain, hearing loss, tinnitus, noise sensitivity, dizziness and equilibrium disorders.
- **Throat:** chronic sore throat, swollen glands, cough, hoarseness, difficulty swallowing
- **Cardio:** weakness, dizziness, irregular heart beats, myocarditis, pericarditis, palpitations, heart block, enlarged heart, fainting, shortness of breath, chest pain, mitral valve prolapse, vasculitis
- **Respiratory:** pleurisy, chest pains, respiratory infections, cough, asthma, pneumonia
- **Abdomen:** pain, diarrhea, nausea, vomiting abdominal cramps, anorexia, liver infection/hepatitis, elevated liver enzymes, enlarged spleen
- **Urinary:** pain with urination, prostate pain, recurrent UTI's, interstitial cystitis
- **Reproductive:** swollen testicles, irregular or ceased menses, galactorrhea,
- **Musculoskeletal:** arthralgias, fibromyalgia
- **Derm:** EM, single or multiple rash, erythema migrans chronicum, hives, ACA
- **Pregnancy:** infertility, miscarriage, premature birth, birth defects, stillbirth
- **Constitutional:** marked fatigue, night sweats, recurrent fevers. Fevers in the afternoon (99.0)

The Alzheimer's and Autism Connection

- **Possible link with Alzheimer's Disease:** ongoing research, not published yet presented at the AANP 2005 annual convention demonstrated that in 10 post-mortem Alzheimer's patients, 7 of specimens had fusion of DNA from the flagellin of Bb with the human DNA of chromosome 11 producing a Transfection product. Samples were taken from the neurofibrillary tangles within the hippocampus and analyzed with PCR and DNA sequencing.
 - In 1913 Noguchi and Moore reported *Treponema pallidum* spirochetes were found in 12 of 70 brains from patient with general paresis.

Lyme and Autism Connection?

- The 15 states with the highest incidence of Lyme disease, 12 of those states have the highest incidence of Autism Spectrum Disorders(ASD). Lyme and ASD's share many common symptoms.
- Recent study by Kuhn, Bransfield and Harris: four male children (ages 26-55 months) with ASD diagnosed and one male child (18 months) who displayed behaviors consistent with ASD were evaluated 6 months prior to ax tx and and after 6 months of ax tx. Each child was prescribed amoxicillin 200mg tid and three of the 5 children were given Azithromycin 50mg QD. All children's scores on SAP-O assessment improved. Noted also was anecdotal data of improved speech, eye contact, sleep behaviors, and a reduction in repetitive behaviors.
- SAP-O: SCERTS Assessment Observation Scale which meets state and federal requirements as ongoing assessment for a child with ASDs.

Diagnosis

- **Strange, but the CDC and the IDSA** still concludes that Lyme disease is a **clinical diagnosis**, but rarely will treat someone with a positive Lyme titer. Figure that one out!
- Patients who are diagnosed by IDSA guidelines are treated typically with 100 mg Doxycycline bid for 2-3 weeks and if they have symptoms after treatment are frequently told that it is "post lyme syndrome" (and not Lyme Disease) even though the researchers who helped develop IDSA guidelines have in their own studies shown positive culture in post treatment symptomatic individuals.

Laboratory Tests

- The **ELISA** test is unreliable, and **misses 35%** of culture proven Lyme (only 65% sensitivity!) and is unacceptable as the first step of a two step screening protocol. (By definition a screening test should have 95% sensitivity.)
- Of patients with acute culture proven Lyme disease, **20-30% remain seronegative** on serial **Western Blot** sampling. Antibody titers also appear to decline over time; thus, the IgG Western Blot is even less sensitive in detecting chronic Lyme infection yet the IgM Western Blot may work.

- **"Two Year Eval of Bb Culture and Supplementary Tests for Definitive Diagnosis of Lyme Disease", Coulter et al; Journal of Clinical Microbiology; Oct 2005, 5080-5084**
- **ILADS annual conference and guidelines**

Laboratory Tests

- For "epidemiological purposes" the CDC eliminated from the Western Blot analysis the reading of **bands 31 and 34**. These bands are so specific to *Borrelia burgdorferi* that they have been chosen for vaccine development. However, for patients not vaccinated for Lyme, a positive 31 or 34 band is highly indicative of *Borrelia burgdorferi* exposure.
- When used as a part of a diagnostic evaluation for Lyme disease, the Western Blot should be performed by a **laboratory that reads and reports on all 16 bands** as part of their routine comprehensive analysis.

Diagnosing Lyme Disease Laboratory Tests Cont.

- Labs that **do** report all 16 bands include Igenex, MDL, Immunosciences.
- If you expect exposure has taken place in another country with other strains, alert the lab.
- PCR on serum, whole blood, synovial fluid and CSF has a sensitivity consistently 20% or less.
- PCR on *Bb* infected rashes has a sensitivity of over 90%.

Western Blot Demystified

| | | IgG | IgG | IgM | IgM |
|-------------|-----------------------|--------------------|----------------|--------------------|---------------|
| Band KDa | Band Importance | ma et al 2 of 6 | CDC 5 of 10 | Ma et al 2 of 5 | CDC 2 of 3 |
| 18 | specific | | x | | |
| 22 | specific | | | | |
| 23-25 | OSP-C highly specific | x | x | x | x |
| 28 | | | x | | |
| 30 | | | x | | |
| 31 | OSP-A highly specific | x | | x | |
| 34 | OSP-B highly specific | x | | x | |
| 37 | specific | | | | |
| 39 | specific | x | x | x | x |
| 41 | non-specific-flagella | x | x | x | x |
| 45 | non-specific | | x | | |
| 58 | | | x | | |
| 66 | non-specific | | x | | |
| 73 | non-specific | | | | |
| 83 | specific | | | | |
| 93 | specific | x | x | | |

Western Blot Demystified

- Western blots look for antibodies. These antibodies are made by your immune system. In this case, the antibodies are made to fight against different parts of the spirochete. In other words, your immune system does not make one big antibody against the whole spirochete. So, when you see a number on a Lyme Western blot, it corresponds to a specific part of the bacteria.

Western Blot Demystified

- Numbers on Western blots correspond to weights. Kilodaltons (kDa) are the units used for these microscopic weights. Think of it like pounds or ounces. An 18 kDa antibody weighs 18 kilodaltons. To do a Western blot, thin gel strips are impregnated with the various parts of *Borrelia burgdorferi*. Each of the numbers, 18 through 93, on the test result form, is a part of the bacteria.

Western Blot Demystified

Serum (a component of your blood) contains antibodies made by the immune system. Electricity is used to push the serum through the thin gel strips for the Western blot. If there are any antibodies against parts of *Borrelia burgdorferi* present in your serum, and these parts are impregnated on the strip, the antibody will complex (bind) to that part.

Western Blot Demystified

In the case of borreliosis, the various parts of *Borrelia burgdorferi* are all antigens. Though each antigen is different, they all come from the same bacteria. So all the numbers that are positive on the test report are due to antigen-antibody complexes.

Western Blot Demystified-tiny details

If enough of the complexes are formed, eventually it may be seen with the naked eye as a dark band. Band intensity reflects how dark or wide it is. Controversy exists about band intensity. Many would say the "+/-" equivocal bands are not significant. The problem I have with that, is that there are "-" negative bands. The lab has no trouble calling some bands negative. So they must be seeing something when they put "+/-" at some bands.

Western Blot Demystified

- The only thing that makes sense, is that there is a little bit of that antibody present in your serum. If the "+/-" equivocal is reported on the borrelia associated bands, it is usually significant, in my clinical experience.

Western Blot Demystified

- Instead of ignoring these, pursue further laboratory diagnosis. OR treat for 4 weeks of antibiotics. This sometimes can convert a negative or equivocal Western blot to positive in about (36% of cases.)
- What may happen when patients are given 4 weeks of doxycycline (or other antibiotics) is that some of the bacteria die. When *Borrelia burgdorferi* dies, it is less efficient at avoiding the immune system. That's when antibodies may be formed against *Borrelia burgdorferi*, converting the negative or equivocal Western blot to positive.
- Wait 3 weeks post AB's to run another western blot.

Reading Western blots

- Bands 31, 34 usually late stage, esp if 83-93 (EVEN IF IGM)
- Bands 41, think co-infections
- Bands 23, 29 58, acute
- IgM in late stage dz, b/c the spirochete hides, and when it comes back it has a new outer surface protein, hence the body thinks that it is a new infection. In addition, every time *Borrelia burgdorferi* reproduces itself, it may stimulate the immune system to form new IgM antibodies.

Western Blot Demystified

- False negative test results are the real problem in diagnosing borreliosis.
- you have to do the right test (the Western blot), done at the right laboratory (one that specializes in testing borreliosis), and done the correct way (shipped express delivery early in the week).

Western Blot

- The Western blot depends on the adequacy of the patient's immune system at the time of exposure.
- If a person is inoculated with a large spirochetal load, immune paralysis can occur.
- By the time the immune system recovers, the spirochete is intracellular, therefore undetected by laboratory tests.
- Early and inadequate Ab treatment may create a false negative.
- Antibodies are tied up in immune complexes
- Borrelia is hiding, or levels are too low
- Patient have a generally low immune system

- (western blots miss 1 in 4 cases)

Lyme Urine Antigen Test

- Lyme Urine Antigen Test (LUAT)
- The LUAT finds the actual antigen (*Borrelia burgdorferi* itself), so arguably it should be the test of choice, but the Western blot is more widely accepted, even though it looks for the antibodies against *Borrelia burgdorferi*.

Chronic Inflammatory Reaction Syndrome (my version of post-lyme syndrome)

If inflammatory markers are high (TGF beta-1, C3a, C4a, MMP-9) and regulatory neuropeptides are low (ADH, MSH, VIP) then consider diagnosis of CIRIS and likely mold involvement.

- Lyme/co-infections more likely if these tests are close to normal and low CD-57 and perhaps elevated C3a or both C3a and C4a.

CD-57

Chronic LB infections are known to suppress the immune system and decrease the quantity of the CD-57 subset of natural killer cells. As in HIV infection, where abnormally low T-cell counts are routinely used as a marker of how active that infection is, in LB we can use the CD-57 count to indicate how active the Lyme infection is and whether, after treatment ends, a relapse is likely to occur.

CD-57

- **When the test is run by Labcorp (preferred lab) you want the test to be above 60; a normal count is above 200. There generally is some degree of fluctuation of this count over time and the number does not progressively increase as treatment proceeds. Instead it will remain low until the LB infection is controlled and then it will jump. If the CD-57 count is not in the normal range when a course of antibiotics is ended, then a relapse may occur.**

CD-57

- The CD-57 can be ordered by your doctor through Labcorp using the following info:
505026 HNK1 (CD57)Panel
- IGENEX. (about 100.00)
- Run before treatment and after treatment.
- For an excellent explanation of the CD-57 read page 8 of the August 2006 issue of Public Health Alert for "All you wanted to know about the CD-57" : <http://www.publichealthalert.org/ArticleAnted.html>

CD-57

- Testing low on this test or below 60 indicates very likely active Lyme Disease.
- Aim for 200 before stopping antibiotics (and remission of all symptoms for 4 full months).

Laboratory Tests Cont.

- Often labs will be normal.
- If you want the most thorough Lyme and TBD workup, I recommend testing through IgeneX, which is an independent (but out of pocket) laboratory. A western blot IgM and IgG is a good place to start.
- Even if these tests come may inconclusive, Lyme or other co-infections may be present. Often times, labs will start to become positive after treatment has begun.
- Leukocytes often are on the very low end of normal, or below normal.

Out of pocket expenses add
up!

You may want to save your money and
treat/challenge with herbs, or even
antibiotics.

An integrated approach

- Never just assume that Lyme is the only thing going on.
- While getting rid of the infection is important, it is also important to strengthen the immune system, treat intestinal dysbiosis, metals and allergies, detoxify and restore hormonal balance.
- If the body is weak or disrupted, then it may not respond to Lyme treatments.

Other labs (these will be covered by insurance)

- TSH often normal, T3 may be low, may not be.
- Sex hormones are often low. (borrelia destroys connective tissue, which is abundant in endocrine glands)
- There is now recognized pathophysiology as to why there tends to be HPA dysfunction with Lyme. Use salivary cortisol testing.
- It is important to supplement thyroid and adrenal dysfunction.

Parasites and Candida

I always run a Complete Digestive Stool Analysis on all of my suspected Lyme patients.

Often times (even in non-Lyme infected patients), there will be a positive test for parasites and/or other fungal elements.

Mold, bacteria and metals

- Borrelia, co-infections, parasites, mold toxins and metals share the same mechanism of actions. They act intra-cellularly to alter cell function.
- They disturb the homeostasis of the endocrine, digestive and nervous system.
- They lead to immune suppression or autoimmunity.
- They affect patients at the hypothalamus, pituitary or peripheral sites.
- They are slow growing and additive
- Though they cause similar symptoms, patients are quite variable in their symptom presentation.

Tick Born Co-infections

There is usually a dominant pathogen. Observe and treat accordingly. The symptom picture will change. The immune system will react to the primary stressor, and depending on the person's strengths and weakness, the symptom picture will emerge.

A typical co-infection panel that I suggest includes:

- *B. microti* and *B. duncani* (WA-1): for Babesia
- *B. henselae* and *B. Quintana* IgM and IgG: for Bartonella
- *Anaplasma phagocytophila* IgM and IgG: for human granulocytic Ehrlichiosis (HGE)
- *Ehrlichia chaffeensis* Ab IgM and IgG: for Human monocytic Ehrlichiosis (HME)

Treat Viruses first

Although not true co-infections, viral infections are often re-activated when Lyme is active, so testing and treating for herpes family viruses, EBV, CMV, as well as *candida* is important.

Babesia

- **Babesia:** intra-cellular Malaria like protozoal organism. Infects red cells. It is thought that 2/3 of Lyme pts have Babesia, which is hard to diagnose as there are over 17 antigen different subspecies and the only current tests cover only *B. microti* and WA-1, which are the most common in western US states.
- **Diagnosis:** via FISH test or WA-1 test through Igenex, MDL or Immunosciences. Some people use long term observation of blood under darkfield microscope as Babesia leaves dying cells which can be observed under darkfield.
- **Treatment:** Rx's: Mepron with Azithromax. Artemisinin (200-300 mg bid 3 wk on/1 wk off taken with grapefruit juice) is used and has been shown in studies to be 20% more effective for malaria than the pharmaceutical treatments. Use with boneset (best way is a hot tea)

Clear Babesia

- Memory and cognition
- Progressive disabling memory
- Gets lost in familiar place
- Can't think linearly
- Severe depression
- Fear and OCD
- Pressure sensation (more than HA) in head and behind eyes.
- Sensations in head, hot spots, numbness, crawling, crown tenderness.

Babesia

- Severe sleep disturbances. Weird dreams and nightmares.
- Temp intolerance, hot and cold with cold dominant. Occasional fever but usually can't get warm.
- Sweats, worse at night.
- Fluid imbalance, overloaded or dehydrated
- Appetite swings

Babesia

- Dizziness, vertigo
- Racing heart, worse at night. PVC's or tachy
- SOB
- Intermittent blurring/ocular migraines
- Tinnitus
- Wrist, hands, ankle and feet: Sensations are different. Usually temperature, but can also be painful, burning or numb.

Bartonella

- **Bartonella:** causative organism is *B. henselae* and *B. quintana*. Also known as "Cat Scratch Disease" as it transmits between humans and cats.
- **Diagnosis:** Antibody or Antigen testing for the organism, best done again through Igenex, MDL, or Immunosciences.
- **Treatment:** Rx's: Levaquin or Septra and Rifampin together; herbal support includes, *Polygonum* and *Stephania* root along with supportive treatment.

Bartonella

- Joint pain: large or small. Wandering, can be swollen. Seldom hot. Often peri-articular
- Headache: can be severe. Ice-pick in and around eyes, migraine. Babesia has more pressure and weird sensations.
- Same cognitive problems, but less disabling.

Bartonella

- Lymphatic system: Mild splenomegaly, boggy lymphadenopathy, seldom hard, but painful. Worse cervical chain, popliteal fossa, puffy supraclavicular (left worse).
- Chest: Painful chest wall, mid/upper sternum. endocarditis
- Eyes: pain in and around eyes, intermittent blurred vision
- Mild sore throat, gastritis, dysmotility, difficulty swallowing.
- Mild hepatomegaly, mildly elevated liver enzymes, gallbladder d/o and GERD. RUQ pain.
- Skin: rashes, papular, stria, abdominal and upper legs, subcutaneous nodules tender, crawling and burning sensations.

Bartonella

- Feet: sensitive and painful soles, worse getting out of bed, usually B/L.
Painful bones of feet, foot and ankle painful, usually U/L.
 - anxiety/psychiatric symptoms,
 - neuropathy/Reflex Sympathetic Dystrophy
 - jaw bone cavitations and devitalized teeth
 - often a co-infection in ALS and fibromyalgia
- Summing up: anxiety (over-riding symptom), with burning neuropathic pain....think Bartonella.

Ehrlichiosis

- **Ehrlichiosis:** human granulocytic Ehrlichiosis (HGE) is caused by *Anaplasma phagocytophila*. Human monocytic Ehrlichiosis (HME) is caused by *Ehrlichia chaffeensis*. Often found in Lyme patients who have contact with horses and farm animals.
- **Diagnosis:** Antibody or Antigen testing for the organism, best done again through Igenex, MDL, or Immunosciences, but the easiest co-infection to test for using conventional testing.
- **Treatment:** Doxycycline 200 mg bid for 1-2 months; astragalus and colchicine

Ehrlichia

- Has slowly progressive neurological presentation.
- Effects extremities more than center of body.
- Neuro symptoms: tingling, numbness, buzzing, burning, shooting for legs or hands. severe pain syndromes
- Has least effect on brain.
- Can have overlapping and synergistic effects on pre-existing conditions, such as TOS, carpal tunnel, sciatica and muscle/tendon pain.
- Ehrlichia often takes back seat if babesia or Bartonella is present.

Ehrlichia

- fever after initial infection
- leukopenia and thrombocytopenia
- Hyponatremia
- mental confusion
- skin rashes – including genital and oral ulcers
- Summer flu, think Ehrlichiosis.

Biofilms

- Spirochetes draw upon calcium, magnesium, iron, heavy metals, fibrin and other elements to weave a protective coat around themselves.
- They create a “filmy” structure around themselves and shed their outer membrane proteins (which serve as antigens), and are able to evade the immune system and antibiotics
- In a biofilm, pathogens are 100-1000 times more antibiotic resistant.

Biofilms (again....)

- To get at spirochetes in the gut, it is important to break down their house, or their “biofilm.”
- This is achieved with high doses of enzymes (which break down fibrin) and a low dose chelating agent (that takes away the protective outer shell of calcium, magnesium and iron).

Focus on other infections and
toxicity exposures.

Remember that we have been exposed to
Borrelia for thousands of years already!

So why are we getting so sick all of a
sudden? We are more burdened and
potentially toxic now.

Natuopathic Approach to Chronic Disease

Clean Up the Home

Clean Up the Body

Fix/treat Biochemistry

Immune Modulation

Decrease Microbial Burden

6) Remove toxic waste/Detoxify

7) Rebuild, repair and restore

Clean Up the Body

- Most have overload of toxins
- Start to deal with metal detox
- Start binding biotoxins and mycotoxins
- Get eliminatory organs functioning optimally,
if possible
- Clean water and food – dietary changes appropriate
to individual

Biochemistry and genetics

Everyone manifests health and illness in their own unique way

- Test for KPU/HPU – will allow for detox of metals and improved immune function
- Methylation dysfunction
- Insulin Resistance
- Not everybody will become chronically ill. Some patients are genetically predisposed to have an autoimmune reaction to Lyme infections. (HLA markers)

Immune Modulation

- Calm the “Cytokine Storm” (aka Herxheimer reaction)
- Homeopathic Lyme and Co-infections Nosodes
- Curcumin, Bromelain, Boswelvia
- Homeopathics
- Low Dose Naltrexone

Decrease Microbial Burden

- Prioritize infections to treat
- In general, parasites (including Babesiosis) and fungal issues need treatment first
- Then viruses and bacteria

We are super-organisms too!

- Research by Dr. J Nicholson supports the view that we are not isolated human genomic organisms, but a symbiote which contains over 3.3 pounds of microbial mass in our gut, with over 10 trillion cells that continuously interact with and modify our genetic phenotype.
- The number of bacteria living within the body of the average healthy adult human are estimated to outnumber human cells, 10 to 1.

We live in their world

- 90% of us is bacterial DNA
- 10% of us is our own DNA
- We need to evolve with these bugs, not simply spray them with pesticides (antibiotics)

Naturopathic Treatment of Lyme Disease

- Customize treatments
- Patient as partner
- Do no harm
- Treat underlying cause
- B vitamins, preferably IM important, often 1+ injections per week
- Minerals very important, as long as fasciculation's (muscle twitches) are present, the dosage needs to be increased, possibly IV or IM.
Often people are zinc, selenium and Magnesium deficient
- liver and bowel support, especially while on antibiotics
- adrenal and all endocrine organ support
- DETOX support to decrease total load. I detox my patients for 4-6 weeks before starting therapy to ensure that they will be able to properly eliminate the spirochete. This prevents the terrible feeling of Herxheimer or "die-off."

Your constitution

- What was your state of health like before the onset of Lyme disease?
- What is the patient's "toxic load" prior to infection? How is their liver and other elimination pathways working?
- How is your attitude, faith and optimism?

Naturopathic Treatment

Some anti borrelial herbs are:

- Uncaria tomentosa (TOA's removed)
 - Teasel root, smilax
 - Andrographis
 - polygonum.
-
- An old formula for Syphilis, which may also be used also with lyme is 1:2 or 1:3 1tsp tid of smilax, stillingia, guaiacum, andrographis, zanthoxylum

Neurotoxins and Elimination

- When a spirochete dies, it empties its contents into the blood. The contents are toxic to the central nervous system.
- It is of great importance that one uses a substance to bind the neurotoxin in order to properly eliminate it from the body (chlorella, clay)

BOTANICAL THERAPIES

- I trust in the plants, and see their importance and powerfulness in the treatment of this disease.
- Though I am an advocate of the use of antibiotics, I don't think that AB's have the ability to fully and permanently heal the patient.
- I think that the best treatment is an integrated and individualized treatment.

BOTANICAL THERAPIES

- Stephen Buhner, wrote an excellent book, called “Healing Lyme,” which focuses on herbal treatments.
- I formulated a tincture with the herbs that he recommends, for ease of usage and compliance. Using tinctures lets me formulate for the individual patient, as some patients have neurological symptoms, some have more musculoskeletal symptoms.....

astragalus

- Build the wei qi, it's a spleen and blood tonic. Good in early Lyme. You can grow it around here, all the pollinators love them. Wait 3 years b/4 harvesting. Strengthens the appetite and digestion. Great as a chemo or radiations adjuvant. Chemo works better with it. Works with the NK cells.
- Closes the door, don't let the robber get stuck inside. (don't take it for chronic infection) Codonopsis is similar, but doesn't lock in the infection. It's more like a vegetable.

Teasel root

Prickly signature, eluethero, nettle, raspberry, teasel are plants that will help you to break something down and weave something new. Used to tease cloth, wool in particular (tapestry). Even with modern day technology, they still use this cuz it knows how to tease cloth. Often used synergistically with solomen seal for musculoskeletal conditions. Mends things that are broken, eclectics say, esp in energetic field. Adrenal pulses will change when using it.

Teasel root

Will cause a herx at over 3 drops three times per day. Start with 1 drop, 3 times per day. You can use this for non-lyme arthritis patients.

For people who had a “use” but lost it.

Gather in the spring before stem comes up, or use the flower essence when the flower comes out.

Andrographis (king of bitters)

Dry and cooling (understatement)

Cardioprotective, and great for brain fog and confusion. Tulsi and Bacopa are also good for this too. Bacopa will also help to relax people and help with sleep.

Arthritic inflammation

Stephania root

This is a vine, grows in china. When eye involvements (can make a mild decoction of the root and make an eyewash once per day, or make a medicated ghee).

Kate Gilday says that it helps with floaters (that and triphala).

Used for neurolyme (Bells palsy, also use St. Joan's wort and Wood betany, milk oat (rebuild myelin sheath).

CORE HERBAL MEDICINES

- This herbal formula is best used in addition to antibiotics. It may also be used for those patients who do not wish to use AB's. Using this formula, pt's relapse far less after AB's are finished.
- The herbs in this formula act as anti-inflammatory, anti-spirochetals and help to alleviate the symptoms of Lyme.
- The core herbs include Andrographis, Cat's Claw and Japanese knotweed.

ADDITIONAL HERBAL MEDICINE

- The addition of symptom-specific herbs will make the formula more effective.
- Cilantro and chlorella (used together for neurotoxin elimination)
- Stephania (neurological Lyme), Smilax and teasel (joint and muscle pain) and artemisia (babesia specific).

POLYGONUM CUSPIDATUM

- Japanese knotweed, is growing everywhere around the valley, rather invasively, which is similar to the way the deer tick has invaded the valley over the last few years. Tap root is extremely deep. Can eat shoots in spring, like rhubarb. One of the last food for the bees! Can help to remediate the soil, often found in old dumps.
- Many patients know this as “resveratrol.” It is a powerful anti-lyme treatment.
- Counters the angiogenesis of Bartonella.
- Cardioprotective and protects the brain.
- In prevention and treatment protocols

Uncaria

Grows in South America, vine. Don't need to harvest the root, the above ground part works just fine. Use stem bark, not root bark.

Joint inflammation and pain.

In prevention and treatment formulas

Can be a little hard on the stomach.

20-40 drops tid of tincture

Smilax, jamaican sarsaparilla

- Lymph clearing and endotoxins. Also moves heavy metals out of the body.

Obstacles to Cure

- Mold exposure and other biotoxin challenges
- Genetics (HLA types)
- Electrosmog
- Scars on or in the body
- Dental- amalgams, opposing metals, infections
- Tonsil infection
- Mental/emotional blockages
- Ancestral traumas/toxins passed on
- Mold, intestinal yeast, metals

Allopathic Treatment of Lyme Disease

- Consult the ILADS website for up to date ILADS & IDSA antibiotic protocol guidelines for various stages of the disease. You can also find Dr. Burruscano's (from the ILADS prospective) guidelines on line.
- If it is an acute onset case PROMPT & AGGRESSIVE Tx with Antibiotics is indicated (I recommend the ILADS recommendations), **if not treated correctly at this crucial stage it can be the difference between getting rid of lyme disease or having chronic/recurrent infection.**

ALLOPATHIC AND NATUROPATHIC INTEGRATION

- I strongly urge patients to use specific herbs, oils and specific dietary changes during the course of antibiotics, to improve immune functioning and decrease the spirochetal load.

Treatment Length

- Many patients with chronic Lyme disease require treatment for 1-4 years, or until the patient is symptom free for a minimum of 4 months.
- Relapses occur and maintenance antibiotics may be required, though if adjunctive herbal medicine and a healthy lifestyle is implemented, relapses are less likely.
- There are no tests available to assure us whether the organism is eradicated or the patient is cured.

PREVENTION IS KEY

- It is my goal to never see a new case of chronic Lyme.
- Through discussion, awareness and education, we can achieve this goal.
- Tick checks and immune wellness is important.
- I have also formulated a “Lyme Prevention” tincture for people to take throughout the spring, summer and fall.

Tick checks



TICK BITE?

- Pull off swiftly and gently with tweezers or a tick spoon.
- DO NOT light it on fire or apply vasoline etc
- Take homeopathic Ledum 1M
- Save tick and have it tested. The longer it was on you, the more likely it can transmit disease.
- www.umass.edu/tick/
- Start doxy or herbs (even before the tick results return) and herbal formula

TICK BITE? (CONT)

- If tick was positive, get tested in 4-6 weeks after initial bite for Lyme and co-infections.
- If tick returns positive, treat with doxycycline 100 mg 2x/day for 4-6 weeks WITH HERBS.
- If tick is negative, rest assured, but monitor yourself for symptoms. Tick testing is very reliable, but not 100%.

Resources

- ILADS "International Lyme & Associated Diseases Society"
- LDA "Lyme Disease Association", www.LymeDisease.org
- CALDA "California Lyme Disease Association" – they print the publication "The Lyme Times" www.lymetimes.org
- www.lymenet.org
- IDSA "International Disease Society of America"
- CDC
- State Departments of Health
- www.neuraltherapy.com for Dietrich Klinghardt's protocols on lyme, and also what he put together for Pharmax to treat lyme
- www.chronicneurotoxins.com
- www.lymephotos.com
- There are good books out there, some for medical professionals, some for patients. The famous author Amy Tan has struggled with chronic lyme and has a book about it. A couple of my favorites from a medical standpoint include
 - "Stealth Pathogens – Cell Wall Deficient Forms" by Lida Mattman PhD
 - "Desperation Medicine" by Ritchie Shoemaker M.D.
 - "An Understanding of Laboratory Testing for Lyme Disease", J Spirochetal and Tick-Borne Diseases, 5:16, 1998
 - Stephen Buhner, "Healing Lyme"

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