

TREATING CHRONIC LYME DISEASE

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TYPES OF LYME DISEASE

- **Early Lyme Disease (“Stage I”)**
 - At or before the onset of symptoms
 - Can be cured if treated properly
- **Disseminated Lyme (“Stage II”)**
 - Multiple major body systems affected
 - More difficult to treat
- **Chronic Lyme Disease (“Stage III”)**
 - Ill for one or more years
 - Serologic tests less reliable
 - Treatment must be more aggressive and of longer duration

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DEFINITION OF CHRONIC LYME

- Ill for more than one year, regardless of whether treatment has been given
- Disease changes character
- Involves immune suppression
- *Less* likely to be sero-positive for Lyme
- *More* likely to be co-infected
- More difficult to treat

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CHRONIC LYME DISEASE- Why are patients more ill?

- Higher spirochete Load
- Development of alternate forms
- Immune suppression and evasion
- Protective niches
- Co-infections

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SPIROCHETE LOAD

- **Low Spirochete Load-**
 - Inapparent infection
- **Increased Spirochete Load-**
 - Symptoms
 - Seropositive

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ALTERNATE MORPHOLOGIC FORMS

- Spirochete form- has a cell wall
 - Penicillins, cephalosporins, Primaxin, Vanco
- L-form (spiroplast)- no cell wall
 - Tetracyclines, Erythromycins
- Cyst?
 - Flagyl (metronidazole), tinidazole
 - Rifampin

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IMMUNE SUPPRESSION BY *Borrelia burgdorferi*

- Bb demonstrated to invade and kill cells of the immune system
- Bb demonstrated to inhibit those immune cells not killed
- The longer the infection is present, the greater the effect
- The more spirochetes that are present, the greater the effect

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PROTECTIVE NICHES

- Within cells
- Within ligaments and tendons
- Central nervous system
- Eye

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DIAGNOSING LYME

- Is a clinical diagnosis- look for multisystem involvement
- 17% recall a bite; 36% recall a rash
- 55% with chronic Lyme are sero-negative
- Spinal tap- Only 7% have + CSF antibodies!
- ELISAs are of little value- do Western Blots
- PCRs- 30 % sensitivity at best- requires multiple samples, multiple sources

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CD-57 COUNT (Natural Killer Cells)

- Low counts seen in active Lyme
- Reflects degree of infection
- Can be a screening test
- Can be used to track treatment response
- Can predict relapse
- Commercially available and covered by insurance!

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WESTERN BLOT IN LYME

- Reflects antibody response to specific Bb antigens- they are reported as numbers called "bands"
- Some bands are seen in many different bacteria- "nonspecific bands"
- Some bands are specific to spirochetes
- Some bands are specific to Bb

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WESTERN BLOT IN LYME

- Positive blot contains bands specific for Lyme
- Specific: 18, 21-24, 31, 34, 37, 39, 83 & 93
- Spirochetes in general: 41
- Nonspecific: All others!
- The more specific bands that are present, the more sure the diagnosis

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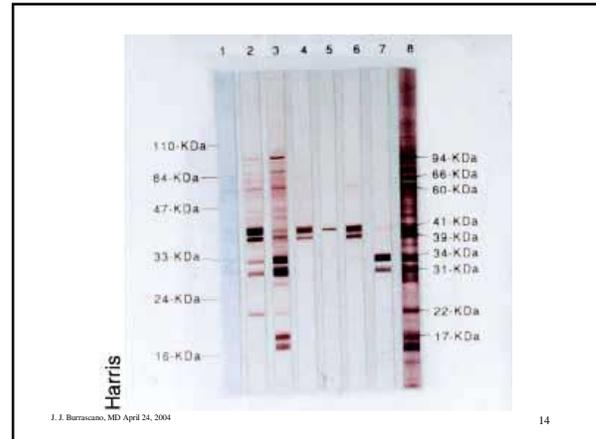
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WESTERN BLOT IN LYME

NOW THE BAD NEWS!

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PITFALLS OF THE WESTERN BLOT

- Very difficult to produce and interpret a western blot
- Bands do not easily line up
- Appearance affected by subtle changes in temperature and chemistry of the test system
- The specific strain of Bb used to produce the antigens may not match the strain the patient has!

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HOW DO YOU MAKE THE DIAGNOSIS?

- *Lyme is a clinical diagnosis*
- *Even the best Lyme tests are only an adjunct*
- *Use the ILADS point system*

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POINT SYSTEM

- Tick exposure in an endemic region 1
- History consistent with Lyme 2
- Systemic signs & symptoms consistent with Bb infection (other potential diagnoses excluded):
 - Single system, e.g., monoarthritis 1
 - Two or more systems 2
 - Erythema migrans, physician confirmed 7
 - ACA, biopsy confirmed 7
 - Seropositivity 3
 - Seroconversion on paired sera 4
 - Tissue microscopy, silver stain 3
 - Tissue microscopy, monoclonal IFA 4
 - Culture positivity 4
 - B. burgdorferi antigen recovery 4
 - B. burgdorferi DNA/RNA recovery 4

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POINT SYSTEM

DIAGNOSIS

- Lyme Borreliosis Highly Likely
– 7 or above
- Lyme Borreliosis Possible
– 5-6
- Lyme Borreliosis Unlikely
– 4 or below

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LYME DISEASE TREATMENT ESSENTIALS

- Pharmacology
- Appropriate route of administration
- Appropriate duration of therapy
- Supportive measures
- Search for co-infections

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LYME DISEASE TREATMENT *Pharmacology*

- Kinetics of killing *B. burgdorferi*
 - Pulse therapy; cell wall agents vs. doxycycline
- Critical to achieve therapeutic drug levels
- Tissue penetration of the antibiotic
- Intracellular site of action
- Alternate forms of *B. burgdorferi*
 - Cell wall agents vs. other mechanisms
- Antibiotic combinations

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ROUTE OF ADMINISTRATION

Repeated Antibiotic Treatment in Chronic Lyme Disease (Fallon, JSTBD, 1999)

- No response to placebo
- Slight benefit from oral antibiotics
- Intramuscular benzathine penicillin more effective than oral antibiotics
- Intravenous therapy most effective

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INDICATIONS FOR INTRAVENOUS THERAPY

- Abnormal spinal fluid (WBC, Protein)
- Synovitis with high ESR
- Illness for more than one year
- Age over 60
- Prior use of steroids
- Failure or intolerance of oral therapy

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ANTIBIOTIC CHOICES: *Oral antibiotics*

- Amoxicillin + probenecid, Augmentin XR
- Doxycycline, minocycline and tetracycline
- Cefuroxime (Ceftin)
- Clarithromycin (Biaxin)
- Azithromycin
- Metronidazole (Flagyl)
- Rifampin

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INTRAVENOUS THERAPY

- Ceftriaxone (Rocephin) still used the most
 - Current recommendation: 2 grams twice a day, 4 days in a row each week
 - more effective
 - safer, and better lifestyle
 - can use peripheral IV line
 - May also prescribe Actigall to prevent gallstones (Bb in gallbladder!)

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INTRAVENOUS THERAPY Other Options

- Cefotaxime (Claforan)
- Doxycycline
- Azithromycin (Zithromax)
- Vancomycin
- Imipenem (Primaxin)

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BICILLIN-LA

- Injection of long acting penicillin-
“Benzathine Penicillin”
- Efficacy is close to that of IV’s!
- 1.2 million U- 3 or 4 doses per week
- No GI side effects and minimal yeast
- Excellent foundation for combination Rx
- Given for 6 to 12 months

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TREATMENT DURATION

- Early infection
 - Four to six weeks to bracket an entire *B. burgdorferi* generation cycle
- Late Infection
 - Open ended therapy that must continue until signs of active infection have cleared
 - IV for 3 to 6+ months, then oral or IM maintenance therapy if tolerated and effective
 - May need to continue treatment for months to years

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KEY POINTS- I

- In chronic Lyme Disease, infection may persist despite prior antibiotic therapy
- Repeated or prolonged antibiotic therapy may be necessary- follow 4-week cycles
- Illogical to follow serologies
- PCR positivity and low CD-57 counts imply persisting, active infection
- Search for co-infections (clinical diagnosis!)

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KEY POINTS- II

- Treat co-infections
- Do not use too low a dose
- Target all morphologic forms of *Borrelia*
- Appropriate route of administration
- Appropriate duration of therapy
- Supportive measures

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CO-INFECTIONS IN LYME

- Nearly universal in chronic Lyme
- Symptoms more vague, and overlap
- Diagnostic tests *LESS* reliable
- Co-infected patients more ill
- Co-infected patients more difficult to treat

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CO-INFECTIONS IN LYME

- Bartonella
- Babesia
- Ehrlichia
- Mycoplasma
- Viruses
- ?Others

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CO-INFECTIONS IN LYME

WHAT IS THE MOST COMMON TICK-BORNE INFECTION IN THE NORTHEAST?

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Bartonella

- More ticks in NE contain Bartonella than contain Lyme
- Clinically, seems to be a different species than “cat scratch disease”
- Gastritis and rashes, CNS, seizures, tender skin nodules and sore soles
- Tests are insensitive! (serologies and PCR)
- Levofloxacin (Levaquin) is drug of choice- consider adding proton pump inhibitor

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PIROPLASMS (Babesia species)

- Many different species found in ticks (13+)
- Not able to test for all varieties
- WA-1 more difficult to treat than B. microti
- Diagnostic tests insensitive
- Chronic persistent infection documented
- Infection is immunosuppressive

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Babesia Testing

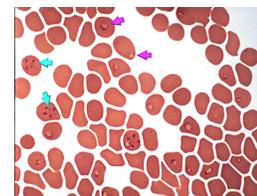
- PCR and Serology
- Fluorescent In-situ Hybridization Assay
 - Fluorescent-linked RNA probe
 - Increases sensitivity 100-fold over conventional Giemsa-stained smears
- Enhanced smears-
 - Buffy coat
 - Prolonged scanning
 - Digital photography

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BABESIA SMEAR

Conventional blood smear

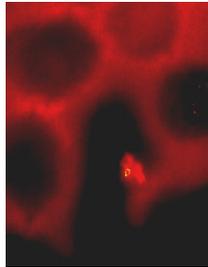


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Fluorescent In-situ Hybridization Assay

Babesia FISH



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Treating Babesiosis

- Is a parasite, so is not treated with antibiotics
- *Can* be treated while on Lyme medications
- Clindamycin + quinine rarely used
- Atovaquone (Mepron) plus azithromycin for 4 to 6 months
- Malarone
- Added sulfur
- Added metronidazole (Flagyl)
- Artemesia

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Ehrlichia

- Can cause acute and chronic presentations
- Acute- sudden high fever, severe headaches, very painful muscles, low WBC counts, elevated liver enzymes
- Chronic- same, but not as severe
- Test with serology, PCR or smear
- Treat with doxycycline or rifampin

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Mycoplasma

- “Chronic fatigue” germ
- Not clear its origin or source
- More often seen in the immunosuppressed
- Test with PCR
- Treat with doxycycline and add fluoroquinolone
- Erythromycins & rifampin, with added hydroxychloroquine OK but less effective

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Other Co-infections

- Especially in the immunosuppressed
- Chlamydiae
- Viruses
 - HHV-6, CMV, other herpes
- Yeasts
- Others

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DANGEROUS MIX!

- Co-infections missed in Lyme patients
- Co-infected patients more ill
- Babesiosis and Ehrlichiosis can be fatal!
- Lyme treatments do not treat Babesia or Bartonella
- One reason for “treatment-resistant” Lyme
- “Silent infections” may be transmitted by transfusions

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ASSOCIATED CONDITIONS

Neurally Mediated Hypotension

- Dehydration, autonomic neuropathy, pituitary insufficiency
- Paradoxical response to adrenaline
 - profound fatigue
 - adrenaline rushes and palpitations
 - unavoidable need to lie down
- Diagnose with tilt table test *performed by a cardiologist*, and pituitary function tests

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ASSOCIATED CONDITIONS

Hormonal Dysfunction

- Significant disturbance of the hypothalamic-pituitary axis
- Extremely difficult to diagnose
- When corrected, are tremendous benefits!
- A major key to the debility in chronic Lyme

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ASSOCIATED CONDITIONS

Hormonal Dysfunction

- Chronic lack of stamina
- Loss of libido
- Intolerance of stress including Herxheimers!
- Unexplained weight gain
- Hypersensitivity to the environment
- Persistent encephalopathy despite Lyme treatment

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ASSOCIATED CONDITIONS

Borrelia Neurotoxin

- Effects
 - Neurologic dysfunction
 - Cytokine activation
 - Hormone receptor blockade
- Testing for neurotoxin:
 - Visual contrast sensitivity test
 - Measure cytokine levels
 - Test for insulin resistance
- Treat with bile acid sequestrants

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ASSOCIATED CONDITIONS

Cerebral Vasculitis

- Contributes to encephalopathy
- Vascular headaches
- Seen on SPECT brain scans

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SPECT BRAIN SCANS

- Reflects blood flow and health of the nerve cells
- Pre and post-Diamox scans
- Proves the symptoms are real!
- Useful in differentiating Lyme Disease from a psychogenic illness
- Can be done serially to reflect clinical changes

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SUPPORTIVE THERAPY

- NUTRITIONAL SUPPORT
 - Blend of multivitamins, B-complex, CoEnzyme Q-10, and magnesium
 - Essential fatty acids
 - Low glycemic index, high fiber diet
 - Absolutely no alcohol
- MANAGE YEAST OVERGROWTH
 - Oral hygiene, acidophilus/yogurt
 - Low carbohydrate diet

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SUPPORTIVE THERAPY

METHYLCOBALAMIN

- Prescription drug derived from vitamin B12
 - Aids in healing the central and peripheral nervous system
 - Documented benefit in strength, energy and cognition
 - Helps restore normal day-night cycle
 - Improves T-cell immune responsiveness
- Must be injected daily for 3 to 6 months
- Available only as a “compounded drug”
- Excellent safety profile

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SUPPORTIVE THERAPY

- ENFORCED REST; NO CAFFEINE
 - Must try to prevent afternoon energy sags
 - Proper sleep is essential
- REHAB AND EXERCISE PROGRAM
 - Required for a full recovery
 - Intermittent program one to three days per week
 - Toning, stretching, posture, balance
 - Aerobics are not allowed until nearly fully recovered

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ALTERNATIVE THERAPIES

THREE CATEGORIES:

- Known to be helpful
- Possibly helpful
- No proven benefit

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ALTERNATIVE THERAPIES

KNOWN TO BE HELPFUL

- Vitamins
 - Multi + Co-Q 10 + B complex + EFAs + Mg
- Hyperbaric oxygen therapy
 - Monochamber preferred; three 30-day dives, one month apart
- Eastern medicinals
- Exercise program

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ALTERNATIVE THERAPIES

POSSIBLY HELPFUL

- Immune modulation
 - Reishi spore extract, transfer factor
 - IVIG only if deficient
- Vitamin C
- Acupuncture

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ALTERNATIVE THERAPIES

NO PROVEN BENEFIT

- Colloidal silver
- Heat therapy
 - Sauna, infrared, hot tubs
- Rife machines

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YOUR DUTY AS A LYME PATIENT

- Political awareness and activity
 - Join support groups and be pro-active
 - Be willing to participate in events
 - Support the major Lyme organizations- ILADS, LDA, LDF
- Fundraising!!!
- Aggressively spread the truth especially to the media
- Never give up, and never go away until our goals are met

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THANK YOU!

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