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

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

CHRONIC LYME DISEASE-
Why are patients more ill?

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

SPIROCHETE LOAD

• Low Spirochete Load-
  – Inapparent infection
• Increased Spirochete Load-
  – Symptoms
  – Seropositive

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
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

PROTECTIVE NICHES

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

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

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!

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

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
WESTERN BLOT IN LYME

NOW THE BAD NEWS!

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!

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

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

DIAGNOSIS

- Lyme Borreliosis Highly Likely
  - 7 or above
- Lyme Borreliosis Possible
  - 5-6
- Lyme Borreliosis Unlikely
  - 4 or below
LYME DISEASE TREATMENT ESSENTIALS

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

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

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

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

ANTIBIOTIC CHOICES:

Oral antibiotics

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

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!)
**INTRAVENOUS THERAPY**

Other Options

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

**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

**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

**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!)

**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

**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
CO-INFECTIONS IN LYME

• Bartonella
• Babesia
• Ehrlichia
• Mycoplasma
• Viruses
• Others

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

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

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

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

BABESIA SMEAR

Conventional blood smear
Fluorescent In-situ Hybridization Assay

Babesia FISH

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

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

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

Other Co-infections

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

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
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

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

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

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

ASSOCIATED CONDITIONS

Cerebral Vasculitis

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

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
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

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

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

ALTERNATIVE THERAPIES

KNOWN TO BE HELPFUL

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

POSSIBLY HELPFUL

• Immune modulation
  – Reishi spore extract, transfer factor
  – IVIG only if deficient
• Vitamin C
• Acupuncture
ALTERNATIVE THERAPIES

NO PROVEN BENEFIT
• Colloidal silver
• Heat therapy
  – Sauna, infrared, hot tubs
• Rife machines

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

THANK YOU!