Clockwise from top: female, male, larva, nymph

Lyme Disease: The Great Stealth Masquerader

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Lyme Disease

- What: the fastest growing vector borne infectious disease in the US, named in 1977 when clusters of children and adults developed arthritis in Old Lyme, CT/Allen Steere, MD

- Where: every state in the union, with highest incidence occurring in the NE, Mid Atlantic states, and Wisconsin (95% of cases in US)

- When: has been present in the US for 100 years boasting 100 different strains/recognized in Europe in the early 20th century/300 strains worldwide/found in 4 continents
Lyme Disease Incidence: 1994-2008

Lyme Disease:
- How (Pathogenesis):
  - Caused by the bite of infected black legged ticks with *Ixodes scapularis* being prevalent in eastern US
  - Ticks have fed from infected reservoirs: white footed mice, other small mammals and birds; these ticks carry an atypical spirochetal bacteria: *Borrelia burgdorferi*

Borrelia burgdorferi (Bb)

*Borrelia burgdorferi* - micrograph (strain B31 in BSK media) after staining with fluorescein isothiocyanate (FITC) and counterstaining with acridine orange. Magnification 600x.
Lyme disease (LD) is a multi-system bacterial infection caused by the spirochete *Borrelia burgdorferi* (Bb). The pathogen was named in honor of the discoverer and a founding board member of the Lyme Disease Foundation, Willy Burgdorfer, PhD, MD (hon.) in 1982.

* Borrelia burgdorferi (the "professional survivor")
  - Isolated in the intestinal tract and salivary glands of black legged tick
  - Mode of motility: using axial filaments endoflagella/move in corkscrew fashion
  - Ability to hide flagella (normally antigenic) from host defenses
  - Only detectable with "Dark-field" microscopy due to narrow width of Bb

* Borrelia burgdorferi (con’t)
  - 1,500 Bb measured end to end=1 inch
  - 100,000 Bb measured side by side=1 inch
  - Can quickly move into circulatory system, passing through capillary walls into body organs, muscles, tendons, ligaments, and joint spaces
  - In animal models, the spirochete can cause a breakdown of the blood-brain barrier within mere hours of tick bite.
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**Borrelia burgdorferi (continued)**

- Over 1500 gene sequences
- At least 132 functioning genes (versus T. pallidum having 22 functioning genes)
- 21 plasmids (three times more than any known bacteria)
- “Stealth” pathology: evades the immune response

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**Borrelia burgdorferi: Stealth Pathology**

- Immune Suppression
- Phase and Antigenic Variation
- Physical Seclusion
  - Intracellular Sites
  - Extracellular Sites
- Secreted Factors

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**LD Transmission Components**

- Lyme disease bacteria (Bb);
- Ticks to transmit the bacteria;
- Suitable relative humidity to support tick life cycle;
- Mammals (mice, chipmunks, deer, etc) to provide food for ticks
- Susceptible prey (humans, domestic animals)
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The changing faces of a deer tick:
Left to Right: unengorged female, 1/4 engorged, 1/2 engorged, and fully engorged

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Available Tests

1) Antibody tests: ELISA & Western Blot serology;
2) Bacterial DNA detection by PCR: testing-amplifies genomic DNA of Bb from skin and body fluids;
3) Antigen detection: finding bacterial particles and proteins in blood, central nervous fluid, and other body fluids;
4) Direct microscopy of tissue and/or body fluids

Problems:

1) Poor sensitivity (65% versus 95%);
2) ELISA tests: not standardized (labs may use different antigens);
3) Migration of spirochete from blood changes immune response;
4) Test timing: early antibody serology will usually be negative
Diagnosis (con’t)

Rashes
- Typical (EM)
- Atypical (more often)
- Allergic reaction to tick saliva

CDC Criteria (Surveillance Case Definition) 1995
- Erythema migrans (physician diagnosed) or
- One to two symptoms of late Lyme disease and
- Positive 2 tier tests (ELISA, Western Blot)

Lyme Disease Surveillance Case Definition: CDC 2008

- Confirmed: 1) A case of EM with a known exposure, or 2) a case of EM with laboratory evidence of infection & without a known exposure, or 3) a case with at least one late manifestation of illness that has laboratory evidence of infection*

Other case classifications: Probable and Suspected

Early Manifestations
(days to weeks after tick bite)

- Erythema migrans – 37% (60-80%)
- Chills – 30-40%
- Fever – 30-40%
- Flu-like symptoms – 50%
- Headache – 40-50%
- Stiff neck – 30-40%
- Myalgias – 40-50%
- Fatigue – 40-50%
Erythema migrans of the right hip

Erythema migrans of the left popliteal region
Emerging EM 1 week post exposure

Mid-Term Manifestations (weeks to months later)

- Meningitis – overall central nervous system (CNS) or peripheral nervous system (PNS) involvement in 10-20%
- Cranial neuropathy – overall CNS or PNS involvement in 10-20%
- Radiculoneuropathy – overall CNS or PNS involvement in 10-20%
- A-V nodal block – overall cardiac involvement 4-10%
- Pericarditis – overall cardiac involvement in 4-10%
- Myocarditis – overall cardiac involvement in 4-10%

Late manifestations (months to years later)

- Arthritis – up to 60% of untreated patients, most often monoarticular and large joint
- Encephalopathy – subtle cognitive dysfunction
- Polyneuropathy – distal paresthesias or radicular pain
System Presentations

- Musculoskeletal
- Neurological
- Visual
- Auditory
- Gastro-Intestinal
- Respiratory
- Cardiac
- General – chronic fatigue
- Psychological

Presentation of LD in Children

**Physical:**
- Fatigue unrelieved by rest, chills, fever;
- Muscle/joint pain, arthritis, decreased muscle tone with balance problems & clumsiness;
- Headaches, stiff necks, dizziness/vertigo, radiating pain & paresthesias, light & noise sensitivity, frequent blinking, tics, visual distortions;

**Neurological/Cognitive Symptoms in Children**

- Short & long term memory deficits;
- Decreased attention span;
- Slowness in word & name retrieval;
- Decreased comprehension & handwriting skills;
- Inability to perform previously mastered mathematical calculations;
- Executive function impairment (inability to activate & sustain effort & attention & manage frustration);
- Frequent errors in speaking, writing, & spelling (dyslexia), declining visual & auditory sequential processing;
Behavioral Symptoms of LD in Children & Adolescents

- Uncharacteristic behavioral presentation: Withdrawal from peers & extracurricular activities;
- New onset of anxiety, OCD, phobias, depression, mood swings, oppositional/defiant behavior, aggressive behaviors with explosive outbursts, panic disorders, sudden onset of suicidal ideation, PDD & autistic-like behavior

Behavioral Symptoms (continued)

Adolescents:
- Often accused of illegal drug abuse d/t symptoms of withdrawal, anxiety, depression;
- Teens may turn to drugs & alcohol to self-medicate their pain;
- Increase in mood swings & oppositional behavior

Who Should be Treated?

- Anyone bitten by a tick which tests positive for spirochetes or,
- A person bitten by a tick and shows symptoms of illness or,
- A person bitten by a tick and is pregnant or,
- A person bitten by a tick who lives in an endemic area
Treatment

- Antibiotics
  - Oral:
    - Amoxicillin plus Probenecid
    - Doxycycline
    - Cefuroxime axetil (Ceftin)
    - Tetracycline (adults only and not in pregnancy)
    - Azithromycin
    - Clarithromycin (Biaxin)
    - Augmentin

Treatment (con't)

- Parenteral Antibiotics
  - Ceftriaxone (Rocephin) IM or IV
  - Doxycycline (requires a central line)
  - Azithromycin (requires central line)
  - Benzathine Penicillin IM
  - Vancomycin (toxicity issues)
  - Primaxin IM or IV
  - Cefuroxime (Ceftin)
  - Ampicillin IV
Treatment (continued)

- Dependent upon drug allergies and tolerance
- Immune Supportive supplements and modalities
  - Probiotics (Entrin)
  - Multivitamins
  - Magnesium L-lactate dehydrate (Mag Tab SR)
  - Vitamin B Complex (50 mg)
  - Vitamin B-12 (500 mcg sublingual)
  - Coenzyme Q10 (up to 300 mg)
  - Essential Fatty Acids (Omega-3, Omega-6)
  - Exercise for re-conditioning
  - Massage therapy, Acupuncture
  - Diet (low sugar, no alcohol)

Alternative Therapies

- Rife Machine
- Hyperbaric Chamber
- Vitamin C & Salt Therapy
- Hyperthermia/Sauna
- Glutathione Replacement Therapy
- Colloidal Silver
- Mercury Detoxification
- Acupuncture

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Treatment (continued)

- Complications
  - Bacterial mutations
  - Forms of Lyme disease
    - Spirochete
    - Spheroblast (L-form)
    - Cystic (can be dormant & then be reactivated)
  - Immune status
  - Co-infections:
    - Babesiosis
    - Ehrlichiosis
    - Bartonellosis
    - Mycoplasma
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**Vaccine for Lyme Disease**

- **History**
  - 1977: First cases of Lyme disease reported
  - 1982: Microbe identified
  - 1989: Outer surface protein, OspA found and cloned
  - Early 1990s: Antibodies to OspA found in CLD patients
  - 1990-1992: Vaccinations with rOspA protected mice against LD
  - 1992-1995: Vaccinations with rOspA tested in other animals
  - 1995: Lyme vaccine found safe and effective in persons with LD
  - 1995-1998: Vaccine found safe and effective in persons without LD
  - 1998: FDA approves Lyme vaccine (LYMErix)
  - 2002: Lyme vaccine withdrawn from market due to poor sales

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**Vaccine (continued)**

- **Efficacy Issues**
  - Vaccinated monkeys: incomplete protection/contracted low level LD infections
  - Human vaccinees: efficacy rate of 49% in first year and efficacy rate of 76% in second year
  - Booster doses necessary due to low titers after two years

- **Purported Safety Issues**
  - Violations of entry & exclusion criteria
  - Vaccine induced autoimmunity (OspA linked to causing treatment resistant arthritic damage in certain genetically vulnerable individuals)

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**Prevention Controls**

- **Engineering Controls**
  - Lawn treatment (permethrin- “Knock-Out”, “Orthomax Insect Killer”)
  - Deer fence
  - Enforced separation lawn-woods
  - Rodent control “Max-Force”
  - “Four Poster Deer Treatment System”
  - Clearing of brush, wood piles, rock walls and birdfeeders
Administrative

- Stay inside
- Move to city

Personal Protection (PPE)

- Light colored barrier clothing;
- Treated clothing: Ex Officio “Buzz Off”, Permethrin sprays & solutions;
- Insect repellents: “Ultrathon” (31.58% DEET), “Skin-So-Soft” Bug Guard Plus (10% Picaridin);
- Inspection of self and family members

Tick Checks

- Check:
  - Behind knee
  - Between fingers and toes
  - Underarms
  - Navel (belly button)
  - Neck, hairline, top of head (use of cool hairdryer)
  - In and behind ear
  - Where underwear elastic touches skin
  - Where bands from pants and skirts touch skin
Tick Removal

1) Grasp tick close to attachment site using fine point tweezers and gently pull straight out;
2) Place tick in closed vial or tape to light colored paper;
3) Have tick identified

Tick Testing Centers

New Jersey Laboratories, New Brunswick, NJ/1-732-249-0148
North American Laboratories, New Britain, CT/1-800-866-NALG
Igenex Laboratories, Palo Alto, CA/1-800-832-3200
Medical Diagnostic Lab, Hamilton, NJ/1-877-269-0090
Clongen Laboratories, LLC, Germantown, MD/1-877-256-6436 **
($75/$195-Borrelia, Bartonella, & Babesia)/3 days

Example: Tick Testing for Lyme Disease & Co-Infections:
$300/10 business days

Lyme Disease and Pets

- Cats: lameness, fever, loss of appetite, fatigue, eye damage/some show no signs
- Dogs: lethargy, loss of appetite, fever, lameness, kidney failure, heart disorders, or neurological involvement (agression), effective vaccine available
- Horses: lameness, joint stiffness, blindness, depression, refusal to eat, neurological signs: head tilt, difficulty swallowing, or aimless wandering
- Cows: lameness, laminitis, fever, swollen joints, weight loss, skin rash on udders; Bb present in frozen milk but killed in pasteurization
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Challenges

- Increasing incidence and morbidity;
- Rising associated health care costs ($60+ million/year);
- Unreliable testing for both detection and disease resolution, and no effective, safe vaccine;
- Inadequate health insurance recognition and support;
- Scientific and medical challenges:
  - Are those with persistent signs and symptoms (CLD) still infected or,
  - Are those with persistent illness dealing with a subsequent autoimmune disease or something else unknown at this time?

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Future

- Increased awareness, early recognition & treatment;
- Research: NINDS: brain imaging & treatment study of adults with late Lyme Disease (chronic) with cognitive problems despite prior IV therapy;
- NIAID: Observational study: ongoing study/1996 consisting of periodic observation or treatment response (blood, u/a, csf, brain imaging, hearing, leukapheresis, neuropsychological testing);
- Recent establishment of the Columbia University Lyme Disease Research Center

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Future (continued)

- Goals: to establish an Advisory Committee & authorize appropriations of $20 million a year for each of 5 years with emphasis on: 1) Research (gold standard diagnostic tests, clinical outcomes research); 2) Examination of current surveillance & reporting; 3) Physician & public education; 4) Prevention
Future (continued)

The LDA has been working with the US Environmental Protection Agency (Office of Pesticide Program) to improve public health by enhancing consumer understanding of the effectiveness of insect repellents (including consistent labeling of pesticides) and the risk of vector-borne diseases.

Future (continued)

The LDA met with officials from the CDC (Dr. Gerberding 2006) and with the Vector-Borne Disease Division of the CDC 8/07 to exchange information & forge collaborative relationships;

NatCapLyme Board met with CDC officials (Ben Beard, PhD & Sarah D. Wiley, MPH) 6/25/09 to discuss inadequate testing, reporting criteria, & ways to increase collaboration.

Special Resources

Lyme Aid 4 Kids:

- Fund initiated & administered by LDA;
- Supported by author Amy Tan;
- Provides up to $1,000 toward diagnosis & treatment for children 21 & under suffering from financial hardship
- Based upon symptoms, history, & recommendation of treating physician/provider
ILADS: Clinician Training Program

- Sponsored by “Turn the Corner Foundation”;
- One to two weeks participation in the care of early and chronic cases of LD, taught by leading Lyme literate physicians;
- Applications: can be downloaded from ILADS website or by contacting Barbara Buchman (Executive Director of ILADS) @ (301-263-1080);
- Stipends ($1500): available but long waiting list

“Freedom to Practice Medicine”

- Provider may prescribe, administer and dispense antibiotics after making a “clinical diagnosis”;
- No provider can be subject to disciplinary action solely for prescribing, administering, or dispensing long term antibiotics by state MEB
- States with protective laws: CT, RI, MA, CA

Resources

- www.aldf.com/FourPosterDeerTreatmentBaitStation.htm
- www.cdc.gov/mmwr
- www.clongen.com
- www.igenex.com
- www.ILADS.org
- www.lymediseaseassociation.org/Lyme-literate/referrals
- www.lymenet.org
- www.lyme.org (LDF) 24* Hotline: 1-800-886-Lyme
- www.Lymetap.org (75% reimbursement*Igenex)
- www.MaxforceTMS.com
- www.mlab.com
- www.MLDA.org
- www.natcaplyme.org
- www.nih.niaid.gov
- www.openeyepictures.com/underourskin/index.html
- www.turnthecorner.org ($$ support/provider training)