

What Doctors Need To Know About

Tick Borne Diseases in the Pediatric Patient

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Tick Borne Disease (TBD)

- All health care providers, mental health professionals and educators in tick endemic areas need to recognize:
 - Growing prevalence of disease after tick bites
 - Clinical manifestations of TBD - protean
 - Children with both acute and persistent TBD so appropriate medical, psychological and educational assistance may be obtained
 - Children diagnosed with neuropsychiatric, learning or attention disorders may indeed have infectious diseases that are treatable

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Tick Bites



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Tick Bites



Pavan WO. *Int J Med Sci* 2009; 6:123
<http://www.medsci.org/v06p0123.htm>

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Endemic Tick Borne Diseases

- Ticks are cesspools of disease
 - *Borrelia burgdorferi*, over 300 strains worldwide
 - Other *Borrelia* species (*lonestari*, *garinii*, *afzelii*, others)
 - *Babesia microti*, *Babesia duncani*, others
 - *Ehrlichia chaffeensis* or Human Monocytic Ehrlichia (HME)
 - *Anaplasma phagocytophilum* or Human Granulocytic Anaplasmosis (HGA)

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Endemic Tick Borne Diseases

- Ticks are cesspools of disease, continued
 - *Bartonella henselae* (cat scratch fever), *Bartonella sp.*, *Bartonella*-like organisms
 - *Mycoplasma fermentans* (Gulf War Syndrome)
 - *Rickettsia rickettsia* or Rocky Mountain Spotted Fever (RMSF)
 - *Francisella tularensis*, or Tularemia
 - *Coxiella burnetii*, or Q fever
 - Viruses (HHV-6, deer tick encephalitis)
 - Nematodes and Protomyxzoa?

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Identifying Children With Lyme Disease

- Lyme is truly the “Great Imitator” of our times just as syphilis was for prior generations
- Onset of the illness can be abrupt or indolent
- All organ systems of the body can be affected
- Symptoms are often vague and shifting from day to day therefore many children are thought to be malingers or be emotionally disturbed
- Children often don't understand what is happening to their bodies and have a hard time explaining often unusual or bizarre symptoms

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Identifying Signs And Symptoms

- How does Lyme disease present?
 - Flu-like illness at any time of the year
 - Fatigue, often unrelieved by rest
 - Unexplained fevers, often cyclical
 - Headaches of all kinds
 - Frequent infections: viral, bacterial and/or fungal
 - Recurrent swollen lymph nodes
 - Recurrent sore throats
 - Chest pains, shortness of breath, dry cough

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Identifying Signs And Symptoms

- How does Lyme disease present? – cont.
 - Abdominal pain of all kinds
 - Changes in appetite
 - Irritable bowel symptoms with changes in stooling patterns
 - Joint pains, migratory and intermittent
 - Deep bone pains
 - Myalgias, muscle spasms and twitches
 - Urinary urgency and frequency, dysuria, incontinence

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Lyme Synovitis - before



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Lyme Synovitis - after



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Identifying Signs And Symptoms

- How does Lyme disease present? – cont.
 - Rashes of all kinds that come and go
 - New onset neurological and/or psychiatric symptoms
 - Sleep disturbances
 - New onset aerobic exercise intolerance
 - Dark circles under the eyes
 - Intermittent red, hot pinnae
 - Increased allergies and chemical sensitivities

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Identifying Signs And Symptoms

- Caveats:
 - Less than 50% of children with Lyme disease remember a tick bite.
 - Even less remember an EM rash.
 - EM rash has highly variable appearance

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Lyme Rashes



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Lyme Rashes



Photo: Edwin Masters, MD and LDA

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In Depth Signs And Symptoms

- Neurological symptoms
 - 90% of children have a deterioration in school performance due to cognitive dysfunction
 - Difficulty with concentration and attention
 - Easy distractibility, often labeled as ADD
 - Word and name retrieval problems
 - Short term memory difficulties
 - Decreased reading comprehension
 - Impaired speech fluency
 - Dyslexic-like errors
 - Loss of mathematical skills

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In Depth Signs And Symptoms

- Neurological symptoms, continued
 - Children with TBD disease demonstrate defects in auditory and visual sequential processing

Tager, Fallon et al. A Controlled Study of Cognitive Deficits in Children With Chronic Lyme Disease. *The Journal of Neuropsychiatry and Clinical Neurosciences* 2001; 13:500-507.

Bloom, Steere et al. Neurocognitive abnormalities in children after classic manifestations of Lyme disease. *Pediatric Infectious Disease Journal* 1998;17(3): 189-196.

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In Depth Signs And Symptoms

- Neurological symptoms, continued
 - Encephalopathy, confusional states
 - Headaches of all kinds
 - Sensory hypersensitivity to noise, light, odors, touch
 - Poor balance and coordination
 - Gait abnormalities
 - Loss of previously acquired motor skills
 - Movement disorders: spasticity, ataxia
 - Motor or vocal tics
 - Convergence and visual tracking problems

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Motor Tic



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In Depth Signs And Symptoms

- Neurological symptoms, continued
 - Spinal cord myelopathies
 - Radiculopathies: Bannwarth's syndrome
 - Peripheral neuropathies: paresthesias, subtle weakness, mild to severely painful
 - Cranial neuropathies: Bell's Palsy, optic neuritis, hearing or swallowing difficulties
 - Autonomic dysfunction: POTS syndrome
 - Partial complex seizures, grand mal seizures
 - Pseudo tumor cerebri

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Bell's Palsy



Left:
May 2007



Right:
May 2009

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Bell's Palsy



April 2011

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In Depth Signs And Symptoms

- Psychiatric Symptoms
 - Uncharacteristic behavior outbursts, mood swings, irritability, emotional lability
 - Social withdrawal, decreased participation in activities
 - Depression
 - Suicidal thoughts in over 40%
 - Rage and anger management disorders
 - Anxiety disorders, panic attacks
 - Depersonalization

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Depersonalization



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In Depth Signs And Symptoms

- Psychiatric Symptoms, cont.
 - Oppositional behaviors
 - Frustration intolerance
 - Obsessive compulsive disorders
 - Hallucinations of all kinds
 - Psychosis
 - Personality changes
 - Self-mutilating behaviors

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Special Age Groups Signs And Symptoms

- Pre-schoolers and toddlers
 - Mood swings, sudden emotional outbursts
 - Irritability
 - Personality changes
 - Return of separation anxiety
 - New phobias
 - Regression of motor and social skills (loss of developmental milestones)
 - Changes in play behavior, tire easily, less active

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Special Age Groups Signs And Symptoms

- Pre-schoolers and toddlers, cont.
 - Trouble falling asleep, frequent awakenings, hard to get them to sleep at night
 - Nightmares, night terrors, sleep walking
 - Diaper rash unresponsive to normal treatment
 - Return to bedwetting or loss daytime bladder control after being dry
 - Frequent URIs, ear and throat infections, bronchitis, pneumonia

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Autistic Spectrum Disorder



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Co-Infections

- Co-infections are the rule, not the exception
 - 80% of my pediatric patients co-infected
 - Co-infections often best diagnosed clinically
 - Co-infected patients are:
 - Sicker
 - More likely to have failed prior treatment
 - Require longer treatment with multiple agents
- Co-infections must be eradicated or *Borrelia* infection will persist

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Signs and Symptoms of Coinfections

- *Babesia* species:
 - High fever with initial infection, later cyclical fevers
 - Night sweats or chills (come in clusters in 1-2 week cycles)
 - Profound fatigue
 - Headache
 - Myalgias
 - Deep bone pains (especially of the distal extremities)

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Signs and Symptoms of Coinfections

- *Babesia* species, continued:
 - SOB, dry cough, chest pain
 - Painful soles of feet
 - Poor balance
 - Severe brain fog/encephalitis
 - Anxiety, panic attacks
 - Chronic low grade anemia, elevated ferritin
 - Hypercoagulability

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Signs and Symptoms of Coinfections

- *Bartonella henselae*:
 - Fatigue
 - Insomnia
 - Headache
 - Abdominal pain
 - Lymph node enlargement
 - Transient soreness of soles of feet upon standing first thing in the morning

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Signs and Symptoms of Coinfections

- *Bartonella henselae*, continued:
 - Psychiatric disorders of all kinds
 - Rage attacks, anger
 - Obsessive compulsive behaviors
 - Cutting/self mutilating behavior
 - Neurological symptoms
 - Resistant radiculopathies
 - New onset seizure disorder
 - Acute encephalitis, disorientation, memory loss
 - Ataxia, tremors

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Signs and Symptoms of Coinfections

- *Bartonella henselae*, continued:
 - Subcutaneous nodules (shins, thighs)
 - Rashes
 - Acne like eruptions
 - “Stretch marks”

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Bartonella Rashes



Photo by Dr. Martin Fried, with thanks to LDA

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Bartonella Rashes



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Bartonella Rashes



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Bartonella Rashes



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Bartonella Rashes



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Signs and Symptoms of Coinfections

- Ehrlichiosis (HME) and Anaplasmosis (HGA):
 - High fevers
 - Flu like symptoms and myalgias
 - Sharp stabbing shooting headache pains
 - Seizures
 - Psychiatric symptoms
 - Low WBC and platelets, elevated liver enzymes

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Signs and Symptoms of Coinfections

- *Mycoplasma fermentans*
 - Fatigue
 - Abdominal pain
 - Myalgias
 - Psychiatric symptoms

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Child Prodigy



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Treatment

- Treatment lasts as long as is necessary
 - Until children are completely symptom free for several months
 - No recurrence of Lyme symptoms with concomitant illnesses or stresses
 - Sickest children often need many months of intravenous, intramuscular and oral antibiotic therapy
 - Children whose diagnosis and treatment are delayed may suffer permanent neurological and physical impairment

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Caveats

- Any child who becomes ill after a tick bite needs a full evaluation for the presence of co-infections
- Any child who becomes ill after a tick bite who was treated with 3 to 4 weeks of oral antibiotics has most likely been inadequately treated
- Initial inadequate treatment makes future treatment more difficult

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Caveats

- Neurological and/or neuropsychiatric signs and symptoms are often the first and only presenting sign of infection
- Neurological and/or neuropsychiatric signs and symptoms are often the most common indication of persistent infection after inadequate treatment

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Selected References

- *Cure Unknown Inside The Lyme Epidemic*
by science writer Pamela Weintraub, senior editor at *Discover* magazine
 - Available at Amazon.com
- *Under Our Skin*
film documentary from Open Eye Pictures directed by Andy Abrahams Wilson
 - Available at Amazon.com
 - www.underourskin.com
 - Trailers on YouTube

Selected References

- Web sites:
 - www.ilads.org
 - The International Lyme and Associated Diseases Society's web site - health care professionals
 - www.lymeinfo.net
 - Educational site with hundreds of medical references
 - www.lymedisease.org
 - Lyme Disease Association web site

Selected References

- Craft, Steere, et al. Antigens of *Borrelia burgdorferi* Recognized during Lyme Disease. Appearance of a New Immunoglobulin M Response and Expansion of the Immunoglobulin G Response Late in the Illness. *J. Clin. Invest.* **1986**; 78: 934-939.
- Andrew Pachner. Neurological Manifestations of Lyme Disease, the New "Great Imitator", *Reviews of Infectious Diseases* **1989**; Vol. II, Supplement 6.
- Krause, et al. Babesiosis: An Underdiagnosed Disease of Children, *Pediatrics* **1992**;89:1045-1048.
- Bloom et al. Neurocognitive abnormalities in children after classic manifestations of Lyme disease, *Pediatric Infectious Disease Journal* **1998**;17:189-96.

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- Tager et al. A Controlled Study of Cognitive Deficits in Children With Chronic Lyme Disease, *The Journal of Neuropsychiatry and Clinical Neurosciences* **2001**;13:500-507.
- Eskow, et al. Concurrent Infection of the Central Nervous System by *Borrelia burgdorferi* and *Bartonella henselae*. Evidence for a Novel Tick-borne Disease Complex, *Archives of Neurology* **2001**;58:1357-1363.

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- Hamlen and Kliman. Lyme Disease: Etiology, Neuropsychological Sequelae and Educational Impact, *Newspaper of the National Association of School Psychologists*. **2007**;35(5):34-36.
- Breitschwerdt, et al., *Bartonella* sp. Bacteremia in Patients with Neurological and Neurocognitive Dysfunction, *Journal of Clinical Microbiology* **2008**;46:2856-2861.
- Breitschwerdt, et al., Molecular Evidence of Perinatal Transmission of *Bartonella vinsonii* subsp. *berkhoffii* and *Bartonella henselae* to a Child. *Journal of Clinical Microbiology* **2010**;48(6):2289–2293.

Appendix 1 - Testing

Two tiered CDC test: ELISA with confirmatory Western Blot (WB)

- Developed for surveillance not diagnosis
- The CDC itself states that it is inappropriate to use surveillance case definitions for
 - establishing clinical diagnoses
 - determining the standard of care necessary for a particular patient
 - setting guidelines for quality assurance
 - providing standards for reimbursement

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Appendix 1 - Testing

Two-tiered CDC test: ELISA with confirmatory WB

- In 1996, New York State Department of Health:
 - found CDC's two tiered testing missed 82% positive Lyme cases
- DeBuono, B. NY Dept of Health report to CDC April 15, 1996
- In 1997, College of American Pathologists stated:
 - commercially available FDA-approved kits were only 36-70% sensitive
 - ELISA assay did not have adequate sensitivity to be part of a two tiered approach to diagnosis
- Bakken et al., *J Clin Microbiol* 1997; 35(3): 537-543

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Appendix 1 - Testing

Two-tiered CDC test: ELISA with confirmatory WB

- In 2005, John's Hopkins University study:
 - found CDC two tiered testing missed 75% of positive Lyme cases

Coulter, et al., *J Clin Microbiol* 2005; 43: 5080-5084

Appendix 1 - Testing

- A CDC positive Western Blot:
 - Requires presence of several non-species specific bands that are common to many spirochetes besides *Borrelia burgdorferi*
 - Omits two of the most species specific *Bb* bands (31, 34)
- A positive Western Blot need only show one species-specific band to demonstrate exposure to *Bb* therefore confirming a clinical diagnosis of Lyme disease
 - These species-specific bands are: 18, 23-25, 31, 34, 39, 83-93 kDa.

Harris, NS. *J Spirochetel Tickborne Dis* 1998; 5(1): 16-26

Appendix 1 - Testing

- Cerebrospinal fluid analysis - mostly normal
“*B. burgdorferi* antigen can be detected in CSF that is otherwise normal by conventional methodology, and can be present without positive CSF antibody. Since CSF antigen implies intrathecal seeding of the infection, **the diagnosis of neurologic infection by *B. burgdorferi* should not be excluded solely on the basis of normal routine CSF or negative CSF antibody analyses.**”

Coyle, PK et al., Detection of *Borrelia burgdorferi*-specific antigen in antibody negative cerebrospinal fluid in neurologic Lyme disease. *Neurology* 1995; 45: 2010-2014

Appendix 1 - Testing

- Cerebrospinal fluid analysis - mostly normal
 - Slightly elevated protein, slight leukocytosis
 - Intrathecal antibodies in less than 9%
 - Only perform tap to rule out other diseases
 - Normal results DO NOT rule out neuroborreliosis

Coyle, PK et al., Seronegative Chronic Relapsing Neuroborreliosis. *Eur Neurol* 1995; 35: 113-117

- One patient with chronic relapsing neuroborreliosis had 13 spinal taps, all PCR or culture positive but only once positive for intrathecal antibody production to Bb antigens.

Coyle, PK et al., *Neurology* 1995; 45: 2010-2014

Appendix 2 - WB Serology

Charles Ray Jones, M.D.

Addendum Regarding Lyme Serology

There are nine known (Lyme) *Borrelia burgdorferi* genus species specific kDa Western blot antibodies (bands): 18, 23-25, 31, 34, 37, 39, 83-93.

Only one of these *Borrelia burgdorferi* genus specific bands is needed to confirm that there is serological evidence of exposure to the *Borrelia burgdorferi* spirochete and can confirm a clinical diagnosis of Lyme disease.

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Appendix 2 - WB Serology

CDC Western Blot IgM surveillance criteria includes only two *B burgdorferi* genus species specific antibodies for IgM 23 and 39 and excludes the other seven *B burgdorferi* antibodies.

CDC Western Blot IgG surveillance criteria includes 18, 23, 30, 37, 39 and 93 and excludes bands 31, 34 and 83.

It does not make sense to exclude any *B burgdorferi* genus species specific antibodies in a Lyme Western Blot, and to include only two of these antibodies in IgM because all the antibodies in IgG were once IgM.

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Appendix 2 - WB Serology

IgM converts to IgG in about two months unless there is a persisting infection driving a persisting IgM reaction. This is the case with any infection, including a *B burgdorferi* induced Lyme disease.

The CDC wrongfully included five non-specific cross reacting antibodies in its Western Blot surveillance criteria: 28.41.45.58 and 66. This leads to the possibility of false positive Lyme Western Blots. There can be no false positives if only *Borrelia burgdorferi* genus species specific antibodies are considered.

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Appendix 2 - WB Serology

One can have a CDC surveillance positive IgG Lyme WB with the five non-specific antibodies without having any *Borrelia burgdorferi* genus species specific antibodies. This does not make sense.

The CDC recommends that the Lyme Western Bolt be performed only if there is a positive or equivocal Lyme ELISA. In my practice of over 10,000 children with Lyme disease, 30% with a CDC positive Lyme Western Blot have negative ELISA's. The Lyme ELISA is a poor screening test. An adequate screening test should have false positives, not false negatives.

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