The Deer Initiative

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Lyme Borreliosis

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Lyme borreliosis is

- Spirochaetal infection found in temperate northern hemisphere
  - *Borrelia burgdorferi* sensu lato

- Tick-transmitted
  - *Ixodes ricinus complex* ticks

PRIMARY PREVENTION: AVOID TICK BITES. Be "tick aware"; highest risk times are late spring, early summer and autumn. Dress appropriately in ticky areas. Insect repellents?

Tick bite risk

- Only a minority of ticks carry borreliae.
- Infected ticks are unlikely to transmit infection if attached for less than 24 hours.

SECONDARY PREVENTION: CHECK FOR TICKS . REMOVE TICKS PROMPTLY - within a few hours. No vaccine available; no early prospect either.

Lyme borreliosis – a few facts

- Estimated *at least* $75 million dollars spent on research during the past 20 years (probably > $100 million).
- Large amount of good-quality science
- Robust diagnosis, treatment, prevention guidelines, 2006
- Laboratory test performances well characterised
- Epidemiological, environmental aspects also well documented
- High profile, despite ***'mystery, little-known illness'*** tag
- ***Large amount of misinformation also available***

Lyme borreliosis is big-business

- 2.7 million tests performed in the USA in 2004
- Very big European market for diagnostics, especially in Germany
- Much of this testing is clinically inappropriate, with dangers from inevitable false-positive results
- Misinformation and quackery helps to drive inappropriate testing, diagnosis and treatment.
- Private sector wacky tests and treatments are rife, expensive and potentially dangerous.

Lyme borreliosis is not new.

Early papers; studies on archived ticks:

- **1883:** ACA (*Buchwald, Germany)*
- **1910:** EM *(Afzelius, Sweden)*
- **1922:** NB *(Garin, Bujadoux, France)*

All described clinical findings of LB

- London (Natural History Museum)
- USA (Smithsonian)
- Museum specimens from Berlin, Munich, Hamburg, Frankfurt, Magdeburg, Vienna

PCR studies on ticks stored from late 19th and early 20th century confirmed presence of borrelial DNA.

LB is:

Produced by a complex interaction between:

Humans: occupational, residential, recreational risks
Ixodes ticks: species and intraspecies variation
Tick feeding hosts: habitat factors, borrelial reservoir competence, extension of deer range etc
B burgdorferi: genospecies, intraspecies variation
Other factors: weather, land use, environmental and climate change?
More prosaically: surburban creep; second homes; new European migration; budget airlines, others.

Borrelia burgdorferi **sensu lato**

Known pathogenic genospecies:

- ***Bb* sensu stricto:** (N America, central Europe, incl Germany). Strongly associated with Lyme arthritis and neuroborreliosis. Rare in UK.
- ***B afzelii:*** widely distributed in Europe, especially Scandinavia. Strongly associated with skin complications. Occurs in UK.
- ***B garinii:*** widely distributed in Europe, including UK; associated with neurological complications.
- ***B valaisiana:*** Western Europe, common in UK; low pathogenicity
- **Other low pathogenic,** eg *B lusitaniae, B japonica, B bissettii*

Clinical features of Lyme borreliosis

- *B burdorferi* genospecies variations
- Host immune response
- Presence of tick borne co-infections? May modify clinical presentations. *(Active case-searching for Anaplasma and Babesia infections, but very few clinical cases found.)*

***Borrelia burgdorferi* infection**

- May be asymptomatic or minimally symptomatic
- May be localised to the skin only
- May affect multiple organs / systems following bloodstream / lymphatic spread

Erythema migrans

- An erythematous lesion which gradually expands from the site of a tick bite
- *may* have a more intense outer border, and a central area which gradually returns to a more normal appearance *(so-called bull's eye rash)*
- onset 3-30 days after a tick bite (average 5-14 days)
- may be accompanied by systemic symptoms, including 'flu-like illness
- Some lesions may become extensive with few or no systemic symptoms.
- Some rashes may be very pale, and easily missed.
- Some rashes may not be seen because of their site, eg on the back.
- Good quality studies suggest that EM rashes occur in about 80% of patients with LB, but some might not have been recognised as such at the time they were present.
- Even without treatment they gradually disappear over weeks or months.
- *Not all rashes occurring after a tick bite are EM.* Consider strep, staph infections; foreign body reactions.

Disseminated Lyme borreliosis

- The organism can spread from the skin to other tissues through the bloodstream and lymphatics.

- This can happen quite early in the infection, but it may take several weeks to several months for complications caused by the organism to become obvious.

- The type of clinical presentation will depend on the organ / system that has been affected

Major organs / systems commonly affected:
- Nervous system
- Musculoskeletal system

Organs / tissues uncommonly affected:
- Heart
- Eye
- Others, including liver, spleen

None of these presentations is unique to LB.

Disseminated LB – Nervous system

- Facial palsy – resolves within weeks, and is not recurrent
- 'Viral-type' meningitis – resolves within days to weeks
- Radiculopathy – variable severity, can be very painful, but starts to resolve rapidly once treatment is given.
- (Bannwarth's syndrome includes all of these features and usually presents within a few weeks to 2-3 months after infection.)
- Other cranial nerve palsies - uncommon
- Encephalomyelitis - uncommon
- Some radiculopathies may come on more slowly and be diagnosed later, up to a year after infection. *(Shingles-type pain)*

Late Lyme borreliosis

- **Acrodermatitis chronica atrophicans** (ACA)
- **Late lyme arthritis** (may be auto-immune element, ie post-infective rather than continuing active infection.)
- **Late neuroborreliosis**
  - axonal polyneuropathy
  - encephalopathy
  - encephalomyelitis
  - peripheral neuropathy associated with ACA

All uncommon, and are very rare in patients who had appropriate earlier treatment.

Long term outcomes of LB

- Numerous outcome studies of treated and untreated LB, and case-control studies
- Interesting German study of patients with *untreated* neuroborreliosis (from 1950s and 60s), showing good outcomes in great majority of patients
- Longest case of persistent Lyme arthritis (initially untreated and had major autoimmune component) resolved within 5 years.
- Patients with untreated active infection for prolonged periods may have incomplete recovery if there has been serious tissue damage (eg severe longstanding ACA or encephalomyelitis)
- *Remember concept of convalescence.* Symptoms may not resolve completely by the end of a treatment course. This does NOT indicate microbiological treatment failure.

Post-Lyme syndromes

Occur only in a small proportion of LB cases (< 5%)

- Persistent subjective symptoms, usually fatigue, musculoskeletal pain, neurocognitive symptoms after LB. These patients usually had more severe systemic symptoms at the initial LB presentation and may have had delayed diagnosis and treatment.
- Chronic fatigue / ME / fibromyalgia-like presentations
- (Preceding LB a trigger factor in rare cases of ME
- ***Reassess history, prior treatment and seek evidence for continuing infection***
- ***No evidence to support multiple or prolonged Abx***

"Unwellness" in general population

- 20-30% adults c/o chronic tiredness *(Refs 248-250)*
- 21.5% adults with doctor-diagnosed arthritis *(251: USA National Health Interview 2003 survey, published 2005)*
- 11.2% point prevalence of chronic widespread pain +/- fatigue, anxiety, depression, somatic symptoms *(252: UK study by Simon Wessely published in 1992)*
- 3.75-12.1% point prevalence self-reported serious pain; 2.17-3.42% emotional or cognitive dysfunction *(253: 2005 USA study)*
- 6.1 self-reported unhealthy days in preceding month *(254: USA 2002 surveillance, published 2005)*
- *How are YOU feeling today?*

Borrelia burgdorferi does NOT cause*:*

- Rheumatoid arthritis

- Polymyalgia rheumatica (PMR)
- Lupus (SLE)
- Scleroderma
- Multiple sclerosis
- Motor neurone disease

Some features of these conditions may have similarities to some found in some patients with LB, but these illnesses are not caused by borrelial infection or other tick borne infections.

Diagnosis of Lyme borreliosis

- History of tick exposure risk
- Clinical presentation compatible with LB ***(None of the later manifestations of LB is unique to Bb infection)***
- A *confidently* made Dx of EM does not require laboratory confirmation.
- Laboratory tests give supporting evidence for clinical diagnosis in disseminated or late LB.

Laboratory tests and LB

- *B burgdorferi* antibody tests are not "Lyme disease tests".
- Low sensitivity in early infection (50-70% within first few weeks)
- Much higher sensitivity in later infection (> 99% in untreated late stage infection)
- Risk of false-positive results, especially with initial screening tests

Tests should not be used if there is no significant chance of disease presence (assess tick exposure risk), as any positive results obtained are highly likely to be false positives.

People who have heavy tick exposure may have true-positive results, but this may reflect past rather than current infection. Significance of results need to be clinically assessed.

Seronegative Lyme borreliosis

- Persons with early infection may be seronegative (ie antibodies are not yet present).
- Late stage seronegativity is rare
    - *Reassess clinical/tick exposure risk history*
    - *Consider additional serological tests*
    - *Is CSF assessment indicated?*
    - *Consider PCR and other investigations*
    - *? Other tick-borne (co-)infections*

Treatment of Lyme borreliosis

IDSA 2006 Evidence-based guidelines

- Oral treatment for most presentations including facial palsy (doxycycline or amoxicillin for 14-28 days)
- IV treatment for other neurological presentations (usually ceftriaxone for 14 days). Some European groups use oral doxycycline 100mg or 200mg twice daily, with good results. Americans are increasingly interested in this option.

NB: Watch erythromycin/flucloxacillin use

Persisting symptoms

- Incorrect diagnosis? *Did the patient have Lyme?*
- Treatment failure? *Right A/B? Right dose / duration? Compliance? Genuine failure?*
- Permanent or slow-to-heal tissue damage? *Usually in later stage of infection at time of diagnosis.*
- Persistent activity of immune response in absence of active infection?
- Intercurrent problem?

Lyme borreliosis – UK picture

- About 600 cases serologically confirmed in 2005
- About 20% acquired abroad *(France, Germany, Austria, Scandinavia, other European countries, USA)*
- UK usual suspects include: New Forest, Thetford, Exmoor, Lake District, Salisbury Plain, parts of the South Downs, rural west Berkshire, Yorkshire moors, Scottish Highlands and Islands, but plenty of others
- *Rule of thumb:* Deer road-signs against a leafy woodland background indicate potential Lyme areas!
- Extension *via* suburban build, deer habitat range, second homes / incomers, recreational pursuits?
  New opportunities for the ticks and the bugs
- Increase in total reports since 2001
- Few late stage presentations each year
- Neuroborreliosis cases steady since 2001:
  - 2001: 53 (32 facial palsies)
  - 2002: 36 (27)
  - 2003: 42 (31)
  - 2004: 58 (30)
  - 2005: 62 (26)
  - 2006 seems to be similar so far.

Suggests greater awareness; Dx and Rx of early Lyme, avoiding later complications.
Numerous awareness-raising activities.

Prevention of Lyme borreliosis

Avoid tick bites

- Education for tick awareness / recognition
- Appropriate clothing in ticky areas
- Insect repellents?
- Environmental controls?
-

Early removal of attached ticks

- Check skin, including skin folds
- Check children's scalps
- Also check clothing and pets' coats for unattached ticks before going back indoors

Vaccine unlikely to be available in the near future; American vaccine has been withdrawn

Post-tick bite prophylaxis not routinely recommended

Most ticks not infected
Consider duration of attachment
Risks v benefits of antibiotics, including modified course of disease

The new world of information, health care and diagnostics

The Internet has brought about many changes

access, empowerment, education
misinformation, quick fixes, quackery
shopping opportunities
responsibilities of vendors and information providers
consumer choices and rights
consumer responsibilities
Health care as a commodity
Caveat emptor

We must learn to live and work with these changes.

Medically unexplained symptoms / chronic illness ME /CFS etc

A huge and largely unmet need for explanation, diagnosis, treatment, management and support – *see newly published Parliamentary report.*

Not a single disease entity
No single trigger
No single management strategy
Many people are desperate for answers

Serious / life-threatening illnesses of unascertained cause

Examples include:

multiple sclerosis
motor neurone disease
other unexplained neurological conditions
scleroderma
systemic lupus erythematosis
polymyalgia rheumatica
cardiomyopathy

Many people are desperate for explanation, support and treatment / cure

Treatments offered by 'alternative' specialists include

Prolonged / multiple repeated courses of oral / iv antimicrobials, including ceftriaxone, macrolides, metronidazole, imipenem, quinolones; atovaquone. ***All can have potentially severe adverse effects.***
Arsenicals; Bismuth iv; Magnesium im; Hydrogen peroxide iv.

- Hyperbaric oxygen; malariatherapy
- Cholestyramine / chelating agents; hydroxychloroquine
- Dietary supplements; herbal extracts
- Rife machines, electromagnetism etc

Mortality and Morbidity

- Few, if any, proven cases of death caused by Lyme borreliosis
- Several deaths from inappropriate treatment
- Large amount of morbidity from inappropriate treatment:
  - including bone marrow aplasia, IV line sepsis, gall bladder problems, enterocolitis, systemic fungal infections, peripheral neuropathy.
- LOSS OF LIFE OPPORTUNITIES, *INCLUDING CHILDHOOD*
- Patients and families also harmed financially.

www.quackwatch.org

Also *www.casewatch.org*

Other good websites:

Centers for Disease Control www.cdc.gov
IDSA: www.idsociety.org

American College of Physicians www.acp.org
American Lyme Disease Foundation www.aldf.org
EUCALB (use google)
HPA: www.hpa.org.uk

Lyme borreliosis – reality and misperceptions

- There are a number of misperceptions about LB.
- Short-hand descriptions of various features do not give a complete picture of the nuances of the condition.
- Deliberate use of inaccurate information and inappropriate tests to support invalid unorthodox approaches to diagnosis and treatment
- In its extreme form, this approach should be considered quackery.
- Serious health protection / consumer protection issues.