



Lyme Disease Action

Lyme Disease: Now you See it, Now you Don't

Dr Sandra Pearson, Medical Director LDA



Personal details

- Medical Director: Lyme Disease Action since 2010. Academic and consultancy role.
sandra.pearson@lymediseaseaction.org.uk
- Lived experience: Husband developed Lyme neuroborreliosis in 2008. My role as carer and advocate.
- Consultant Psychiatrist: Honorary contract Devon Partnership NHS Trust, Member of Royal College of Psychiatrists. CCST General Adult Psychiatry.
- Member of ESCMID: European Society for Microbiology & Infectious Diseases.
- Social media: Twitter @PearsLDA



Lyme Disease Action

- A charity founded by a group of scientists in 2003. 100% funded by voluntary contributions.
- Serving patients, clinicians and researchers.
- Striving for the prevention and treatment of Lyme disease and other tick borne diseases.
- Web-site: <http://www.lymediseaseaction.org.uk/>
Accredited to NHS Information Standard.
- Facebook: <https://www.facebook.com/pages/Lyme-Disease-Action/122058224483868>
- Twitter: @LymeAction



Introduction

- Lyme disease
 - Cause
 - Epidemiology & risk Factors
 - Clinical presentation
 - Laboratory tests
 - Diagnosis
 - Treatment
 - Prevention
- Uncertainties
- Way forward



What is Lyme Disease?

- An infectious disease caused by the bacterium *Borrelia burgdorferi* – a spirochaete
- Discovered in 1981
- Obligate parasite
- Zoonosis
- Transmitted to humans by the bite of an infected tick



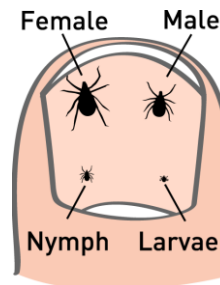
CDC Public Health Image Library



LDA Image Library



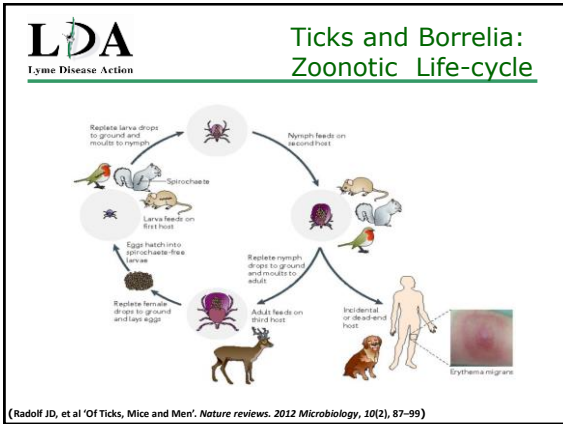
Ticks



Hard bodied ticks:
Ixodes ricinus
Ixodes hexagonus
Ixodes canisuga



Endemic throughout UK



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Tick Feeding 1

Risk zones:

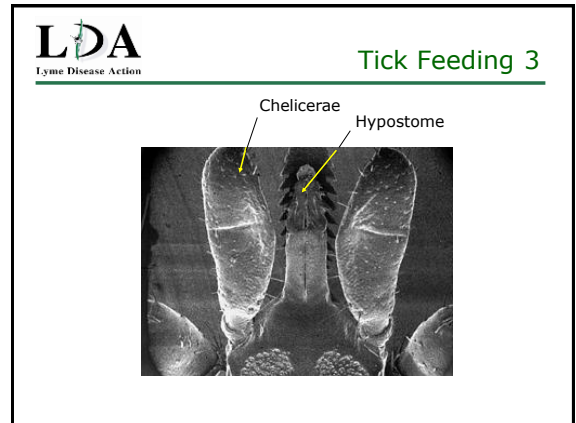
- Woods
- Long grass
- Undergrowth
- Moors & Heathland

Across the UK:
Town and Country!

Tick bites are painless and can go unnoticed

Ticks carry & transmit other pathogens eg Anaplasma, Rickettsiae, Viruses etc.

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Borrelia burgdorferi

The pathogen responsible for Lyme disease: a spirochaete: corkscrew shaped bacterium.

Most common vector-borne Disease in N Hemisphere.

CDC Public Health Image Library

Borrelia burgdorferi sensu lato:

- *B garinii* - Europe
- *B afzelii* - Europe
- *B burgdorferi* - Europe, N America
- *B spielmanii* - Europe

Different species may account for varying disease profiles.

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Borrelia: survivability

- Immunosuppressant properties of Tick saliva.
- Borrelia: Variation outer surface proteins/antigenic expression. VlsE protein.
- Slowing the rate of replication – sacrificing virulence for persistence. Dormancy.
- Protein binding - immune evasion, dissemination, tissue tropism, binding to extra-cellular matrix.
- Sequestration in immune privileged sites eg. beyond BBB.
- Immune dysfunction: Dissociation of T & B cell responses.
- Immune modulation – Th1/Th2 responses>Tolerance.

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Epidemiology- UK

UK Lyme disease Laboratory confirmed cases

- M=F
- Occurs any age
- 45-64 year-old
- Southern counties
- Scottish Highlands
- March – September
- Bimodal distribution

Occurs throughout the UK

- Approximately 10-15% acquired abroad
- Under-reported
- True incidence (x10-20?)

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Epidemiology – Europe 1

Number of Lyme disease cases in Europe as reported to WHO Centralized information system for infectious Diseases (CisID)

Lyme Borreliosis in Europe:
<http://www.ecdc.europa.eu/en/healthtopics/vectors/world-health-day-2014/Documents/factsheet-lyme-borreliosis.pdf>

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Epidemiology – Europe 2

Country	per 100,000 population 10 year average
Slovenia	155
Austria	130
Sweden (south)	80
Netherlands	43
USA high prevalence states	31
Switzerland	30
Germany	25
France	17
Norway	3
United Kingdom	0.7

Probable under-reporting

2009
E & W 1.8
Scotland - 11

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Increasing incidence

- Climate change.
- Changes in land management.
- Changes in biodiversity.
- Changes in human interaction with nature eg. outdoor leisure activities.
- Increasing awareness.

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Clinical features

- Multi-system disorder.
- Borrelia: Tropism, collagen-rich tissues.
- Skin, nervous system, joints heart and eyes.
- May affect any organ of the body.
- 20-30% European cases: Lyme neuroborreliosis.
- USA: Arthritis more common than in Europe.

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Erythema migrans

- Pathognomonic Bull's eye rash
- 3-30 days after the bite
- May not be circular
- May be multiple
- May not be at bite site
- 1 in 3 recall tick-bite
- 65% notice EM rash

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What are the symptoms?

<p>Acute Disseminated (days/weeks)</p> <ul style="list-style-type: none"> • Feeling unwell or 'flu-like • Profound fatigue/malaise • Headache, stiff neck • Fleeting myalgia/arthralgia • Sound/ Light sensitivity • Early neuro symptoms: Facial palsy, diplopia • Heart Block due to Lyme carditis 	<p>Late Disseminated (>4-6 months)</p> <ul style="list-style-type: none"> • Neurological: 15 - 20% Bannwarth's syndrome • Rheumatological: Arthritis • Dermatological: Acrodermatitis Chronicum Atrophicans, Lymphocytoma • Cardiac • Ophthalmic: uveitis
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Stanek G et al (2011) *European Society of Clinical Microbiology & Infectious Diseases*, 17(1):69-79

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The New Great Imitator

- Amyotrophic Lateral Sclerosis (ALS)
- Anxiety
- Arthritis
- Autoimmune conditions
- B12 Deficiency
- Bell's Palsy
- Chronic Fatigue Syndrome (CFS)
- Dementia
- Delirium
- Depression
- Diabetes
- Fibromyalgia
- Guillain-Barré syndrome
- Migraine
- Motor Neurone Disease (MND)
- Multiple Sclerosis (MS)
- Myalgic Encephalomyelitis (ME)
- Parkinson's disease
- Polymyalgia Rheumatica (PMR)
- Poliomyelitis-like syndrome
- Seizures
- Stroke
- Tendonitis
- Tension Headache
- Thyroid Disease
- Vasculitis

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Clinical Diagnosis

Evaluation of risk factors and clinical presentation:

1. Exposure to ticks
2. Tick bite: only 1/3 recall this
3. EM rash: 65%
4. Pattern of symptoms & signs.
5. Seasonal Pattern
6. Outdoor pursuits
7. Occupational groups
8. Companion animals
9. Evaluation of test results

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Laboratory diagnostics 1

- **No gold standard test** in routine clinical use.
- No marker of disease activity.
- **No test of cure.**
- No test to reliably exclude Lyme disease.

Direct Tests:

Culture difficult: Borrelia is a fastidious, slow-growing organism.

Molecular diagnostics: **PCR insensitive** due to low numbers of Borrelia in body fluids & tissues. Same for microscopy.

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Laboratory diagnostics 2

Indirect tests measuring antibody response: 2-tier serology.

1. ELISA/ C6 EIA screening test.
2. Immunoblot (ViraStripe).

- False positives: Cross reactions: IgM, p41 flagellar protein.
- False negatives: Testing too early.
 - Early antibiotics→abrogated immune response.
 - Heterogeneity of European strains.
 - Commercial tests: Lack standardisation.
 - Antigenic variation by Borrelia eg. VlsE.
 - Borrelia evades & disrupts immune response.

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Treatment

- Treatment is with antibiotics
- **Early treatment is more likely to be successful**
- Erythema migrans should be treated without waiting for a blood test (which may be negative)

Early diagnosis

- Typically official view is 2-3 weeks of antibiotics
- usually complete recovery

Late diagnosis

- Longer term treatment may be necessary (controversial).
- Re-treatment may be necessary.
- 15-25% Residual symptoms ?cause.
- Recovery may take time.

Jarisch-Herxheimer reaction may complicate treatment.

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Prevention

- Tick bite prevention.
- Prompt effective tick removal.
- Currently no safe effective vaccine for use in humans.
- Awareness raising: Public and Medical Profession.

<http://www.lymediseaseaction.org.uk/about-ticks/tick-bite-risk-reduction/>

<http://www.lymediseaseaction.org.uk/about-ticks/tick-removal/>

<http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/Ticks/TickPreventionAndRemoval/>

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Removal

As soon as possible!

Do NOT


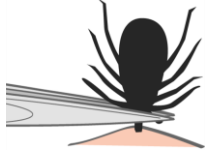
- use oil or nail varnish
- squeeze the tick
- use fingernails

Do

- use a tool

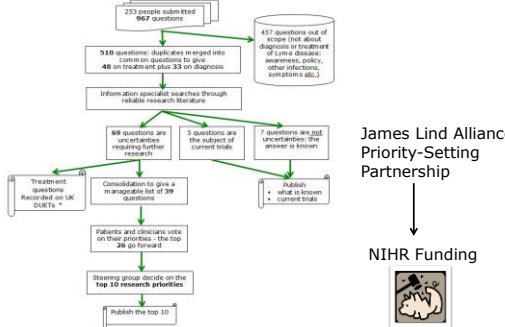
In emergency:

- slit in credit card
- loop of thread

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Uncertainties: JLA 1



253 people submitted 967 questions

518 questions: duplicates merged into common questions to give 48 on treatment plus 33 on diagnosis

457 questions out of scope (not about diagnosis or treatment of Lyme disease, awareness, other infections, symptoms etc.)

Information specialist searches through reliable research literature

69 questions are uncertain (requiring further research)

5 questions are the subject of current trials


7 questions are 'ask' (answer is known)

James Lind Alliance Priority-Setting Partnership

NIHR Funding

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Uncertainties: JLA 2



- Harvested the uncertainties
- Checked for known uncertainties
- Prioritised the shortlist of uncertainties
- Publicised the priorities: UK Duets (treatment), University of Birmingham database (epidemiology)

↓

- An informed research programme
- UK guidelines

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JLA Top 10 Uncertainties

1. Best treatment for children/adults a) early Lyme disease without neurological involvement b) late Lyme disease?
2. Key questions (clinical and epidemiological) to help make a diagnosis of Lyme disease?
3. How effective are current UK tests?
4. Outcomes studies: long term treatment?
5. Relapse. Management?
6. Persistent symptoms: Management?
7. Continuing symptoms: Continued infection, immune dysfunction or other process?
8. How common is relapse and treatment failure and is it related to disease stage, gender, co-infections or any other factor?
9. Are there long-term consequences if treatment is delayed?
10. Can Lyme be transmitted via other means: person to person sexually; trans-placentally; by breast feeding; organ donation or blood products?

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Issues leading to Uncertainty


- **Borrelia** - fastidious, slow replication, difficult to culture, exploits immune privileged sites, dormancy, heterogeneity of strains, immune evasion and disruption.
- **Co-infections** - ?Effect.
- **Immune response** - complex and not fully understood.
- **Tests** - Problematic: no gold standard, no marker of disease activity, no test of cure.
- **Remaining symptoms** - ?persistent infection, ?immune dysfunction or ?tissue damage.
- **Research** - studies variable quality or non-existent, animal models, lack of clearly defined end-points, bias, extrapolation of results.
- **Socio-political aspects** - Inappropriate activism: -> marginalisation 'illuminating History' <http://www.youtube.com/watch?v=uXyHYQVoa84>



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Fallout

- Guidelines/Guidance....IDSA 2006, AAN 2006, ILADS , EFNS 2010. Opinion based where evidence lacking.
- Conflict between guidelines IDSA vs ILADS.
- Divisive splitting - professionals and patients.
- Distorting effect - Literature bias, false claims, 'hyp'.
- Chilling effect on research, medical practice, scientific thinking and debate.
- Stigma, prejudice and marginalisation of Lyme disease.




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Guidelines


European Federation of Neurological Societies 2010

- Early LNB:** "There are no class I comparisons of different treatment durations".
- Late LNB effective agents:** "there are no randomized treatment studies of European late LNB".
- Late LNB treatment duration:** "There are no comparative controlled studies of treatment length in European late LNB"

CKS NHS Clinical Knowledge Summaries
For anything other than erythema migrans "consult an expert"




"In the absence of current consensus, consult with Lyme experts"



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Way forward

- Development of appropriate UK guidance
- Improved awareness & education: RCGP online CPD module, hiblo TV, LDA web-site, updated PHE web-site, via social media.
- Patient and public participation.
- Open dialogue. Rebuilding trust
- Specialist service development
- Enhanced care and treatment
- Sound research



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Summary

- Lyme disease: An increasing Public Health concern
- Clinical Diagnosis : 'Building a diagnosis'
- Diagnostic certainty may not be possible
- Laboratory tests all have their limitations
- Early treatment has best chance of success
- Core uncertainties remain and research is ongoing
- Need improved research
- UK Guidance



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Web-site: Useful Links

For clinicians

Resources

For the public

For employers

For travellers

Diagnosis

Research papers

Off the shelf

Latest News

Quick Links

Latest News

Parliamentary question - 1st 22nd

PHE Lyme disease conference 2013 - 14th

PHE Lyme disease conference announced

Agency advice on carrying a tick

NHS Lyme disease clinic

Conference advice and feedback

E-mail: medics@lymeseason.org.uk



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Thank you for listening



Please visit us at Stand B44!