Lyme disease - information for clinicians

Information Sources and Key Research Evidence

Contents

1. Guidelines and e-learning

- Lyme disease | Guidance | NICE
- Lyme disease | Health topics A to Z | CKS | NICE
- Lyme disease | Quality standards | NICE
- Lyme Disease Toolkit | RCGP Learning
- Summary of Lyme Disease | RCGP Learning
- Lyme disease – UK Health Security Agency
- Lyme disease: sample testing advice - GOV.UK
- Lyme Disease - PAEDIATRIC INNOVATION, EDUCATION & RESEARCH NETWORK
- Lyme disease: Antibiotic choices - BMJ Visual summary
- LRC - Lyme disease awareness for under 12yr olds (children's animation)

2. UK epidemiology

- Cairns V, Wallenhorst C, Rietbrock S, et al, **Incidence of Lyme disease in the UK: a population-based cohort study**, BMJ Open 2019;9:e025916. Doi: 10.1136/bmjopen-2018-025916. https://bmjopen.bmj.com/content/9/7/e025916
- Distribution of Ixodes 2icinus across Great Britain https://assets.publishing.service.gov.uk/media/667bf5f75b0d63b556a4b391/Tick-_Ixodes-ricinus_-distribution-map-for-England-Scotland-and-Wales.pdf

3. Microbiology and immune evasion

- Bamm VV, Ko JT, Mainprize IL, Sanderson VP, Wills MKB. **Lyme Disease Frontiers: Reconciling *Borrelia* Biology and Clinical Conundrums.** Pathogens. 2019 Dec 16;8(4):299. doi: 10.3390/pathogens8040299. PMID: 31888245; PMCID: PMC6963551. https://pubmed.ncbi.nlm.nih.gov/31888245/
- Cook MJ, Puri BK. **Commercial test kits for detection of Lyme borreliosis: a meta-analysis of test accuracy**. *Int J Gen Med*. 2016;9:427-440 https://doi.org/10.2147/IJGM.S122313

4. Signs and symptoms of Lyme disease

(a) Facial Palsy

https://www.sciencedirect.com/science/article/abs/pii/S0165587620300471
High frequency of paediatric facial nerve palsy due to Lyme disease in a geographically endemic region. Munro APS, et al. Int J Pediatr Otorhinolaryngol. 2020 May;132:109905. doi: 10.1016/j.ijporl.2020.109905.
"In areas endemic with Lyme disease, Lyme disease should be considered as the likely cause of facial nerve palsy in children until proven otherwise."

(b) Skin Manifestations

(i) Erythema Migrans (EM) rashes - images

(1) EM rash - white skin

- https://www.nice.org.uk/guidance/ng95/resources/lyme-disease-rash-images-pdf
- **Lyme Disease in 2013: Lessons Learned in Diagnosis,** presentation by John N. Aucott, M.D. (contains multiple examples of EM rash) https://www.childrenslymenetwork.org/files/research/centers-and-institutes/mid-atlantic-public-health-training-center/_documents/051513_lyme_disease_aucott.pdf
- https://phil.cdc.gov/Details.aspx?pid=14471
- Eriksson P, Schröder MT, Niiranen K, Nevanlinna A, Panelius J, Ranki A. **The many faces of solitary and multiple erythema migrans.** Acta Derm Venereol. 2013 Nov;93(6):693-700. doi: 10.2340/00015555-1549. PMID: 23450303.

https://www.medicaljournals.se/acta/content_files/files/pdf/93/6/3872.pdf (scroll to page 696)

- https://europepmc.org/articles/PMC5588623/figure/F3/ (Hofmann H, Fingerle V, Hunfeld KP, et al. **Cutaneous Lyme borreliosis: Guideline of the German Dermatology Society.** German Medical Science : GMS E-journal. 2017 ;15:Doc14. DOI: 10.3205/000255. PMID: 28943834; PMCID: PMC5588623.)
- https://europepmc.org/articles/PMC5588623/figure/F2/ (Hofmann H, Fingerle V, Hunfeld KP, et al. **Cutaneous Lyme borreliosis: Guideline of the German Dermatology Society.** German Medical Science : GMS E-journal. 2017 ;15:Doc14. DOI: 10.3205/000255. PMID: 28943834; PMCID: PMC5588623.)

(2) EM rash - melanated skin

- https://phil.cdc.gov/Details.aspx?pid=14482
- Fathi, R., Huang, W. W, & Brown, K. (2012). **Disseminated Lyme Borreliosis preceded by hepatitis in an African American male**. *Dermatology Online Journal*, 18(10). http://dx.doi.org/10.5070/D39d7813rh Retrieved from https://escholarship.org/uc/item/9d7813rh
- Dennison, Rebekah, et al. **'Lyme Disease with Erythema Migrans and Seventh Nerve Palsy in an African-American Man'**. *Cureus*, vol. 11, no. 12, p. e6509. *PubMed Central*, https://doi.org/10.7759/cureus.6509

(3) Disseminated EM rashes

- https://europepmc.org/articles/PMC5588623/figure/F5/ (Hofmann H, Fingerle V, Hunfeld KP, et al. **Cutaneous Lyme borreliosis: Guideline of the German Dermatology Society.** German Medical Science : GMS E-journal. 2017 ;15:Doc14. DOI: 10.3205/000255. PMID: 28943834; PMCID: PMC5588623.)

***(ii) Late skin manifestations* (acrodermatitis chronica: oedematous infiltrative / atrophic)**

- https://europepmc.org/articles/PMC5588623/figure/F6/ (Hofmann H, Fingerle V, Hunfeld KP, et al. **Cutaneous Lyme borreliosis: Guideline of the German Dermatology Society.** German Medical Science : GMS E-journal. 2017 ;15:Doc14. DOI: 10.3205/000255. PMID: 28943834; PMCID: PMC5588623.)
- https://www.researchgate.net/figure/Acrodermatitus-chronica-atrophicans-A-Acrodermatitis-chronica-atrophicans-of-the-right_fig3_235418752 Deluca, J., Eisendle, K., & Zelger, B. (2013). **Cutaneous and systemic Lyme disease**. *Expert Review of Dermatology*, *8*(1), 65–82. https://doi.org/10.1586/edm.12.71, https://www.researchgate.net/profile/Klaus-Eisendle/publication/235418752_Cutaneous_and_systemic_Lyme_disease/links/02e7e5163b6f43f9dc000000/Cutaneous-and-systemic-Lyme-disease.pdf

(c) Borrelial lymphocytoma

- https://europepmc.org/articles/PMC5588623/figure/F4/ (Hofmann H, Fingerle V, Hunfeld KP, et al. **Cutaneous Lyme borreliosis: Guideline of the German Dermatology Society**. German Medical Science : GMS E-journal. 2017 ;15:Doc14. DOI: 10.3205/000255. PMID: 28943834; PMCID: PMC5588623.)

- Glatz M, Resinger A, Semmelweis K, Ambros-Rudolph CM, Müllegger RR. **Clinical spectrum of skin manifestations of Lyme borreliosis in 204 children in Austria.** Acta Derm Venereol. 2015 May;95(5):565-71. doi: 10.2340/00015555-2000. PMID: 25366035. https://pubmed.ncbi.nlm.nih.gov/25366035/
- Stinco G, Ruscio M, Bergamo S, Trotter D, Patrone P. **Clinical features of 705 Borrelia burgdorferi seropositive patients in an endemic area of northern Italy.** ScientificWorldJournal. 2014 Jan 16;2014:414505. doi: 10.1155/2014/414505. PMID: 24550705; PMCID: PMC3914583. https://www.researchgate.net/figure/Lymphadenosis-benigna-cutis_fig3_260254354

(d) Neuroborreliosis

- *"In total, 26 children were included. The median age was 8 years (4-14 years). The different neurological symptoms reported were: meningoradiculitis (62%), which was usually associated with facial palsy (54%); isolated facial palsy (15%); isolated meningitis (8%); polyradiculoneuritis (4%); benign intracranial hypertension (4%) and myelomeningoradiculitis (4%). The most common functional symptoms were headaches (54%), the perception of asthenia (42%), neck pain (27%), and a loss of appetite (19%). Patients with laboratory meningitis (84%) often had no signs of meningism or headaches (38%)."*
  Lyme neuroborreliosis in pediatrics: A retrospective, descriptive study in southwest France. Garrabe E, et al. Arch Pediatr. 2021 Oct;28(7):537-543. doi: 10.1016/j.arcped.2021.08.001. https://www.sciencedirect.com/science/article/abs/pii/S0929693X2100141X

- **"***The infection occurs in children and adults, but the clinical manifestations differ. In adults, painful meningoradicultis is the most common manifestation of LNB, while children often present with facial nerve palsy and/or subacute meningitis. Subacute headache can be the only manifestation of LNB in children, especially during the summer months in Lyme disease-endemic regions. Non-specific symptoms, such as loss of appetite, fatigue or mood changes, may also occur, especially in young children. A high level of suspicion and early recognition of the various clinical manifestations presented by children with LNB is essential to minimize delay in diagnosis and optimize management."*
  Clinical manifestations of Lyme neuroborreliosis in children: a review. Bruinsma RA, et al. Eur J Pediatr. 2023 May;182(5):1965-1976. doi: 10.1007/s00431-023-04811-w. https://pubmed.ncbi.nlm.nih.gov/36856886/

- **Lyme Neuroborreliosis in Children.** Kozak S, et al.Brain Sci. 2021 Jun 7;11(6):758. doi: 10.3390/brainsci11060758. PMID: 34200467; PMCID: PMC8226969. https://pmc.ncbi.nlm.nih.gov/articles/PMC8226969/

- **The underdiagnosis of neuropsychiatric Lyme disease in children and adults.** Fallon BA, et al. Psychiatr Clin North Am. 1998 Sep;21(3):693-703, viii. doi: 10.1016/s0193-953x(05)70032-0. https://www.sciencedirect.com/science/article/pii/S0193953X05700320

- *"In total, 469 children diagnosed with LD were included (median age, 7.9 years); 190 patients (40.5%) with Lyme neuroborreliosis (LNB), 171 (36.5%) patients with skin manifestations (erythema migrans, n = 121; multiple erythema migrans, n = 11; borrelial lymphocytoma, n = 37; and acrodermatitis chronica atrophicans, n = 2), and 108 (23.0%) patients with Lyme arthritis. We observed seasonal variations for patients with skin manifestations and LNB, with high prevalence in May–October, but not for patients with Lyme arthritis. Significant differences between LD manifestation groups were found for age, inflammatory parameters, and specificity and concentration of B. burgdorferi-specific serum antibody responses."*
  Clinical characteristics and serological profiles of Lyme disease in children: a 15-year retrospective cohort study in Switzerland. Greiter BM, et al. Lancet Reg Health Eur. 2024 Dec 9;48:101143. doi: 10.1016/j.lanepe.2024.101143. https://pubmed.ncbi.nlm.nih.gov/39736882/ https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762%2824%2900312-0/fulltext

- *"Clinical presenting signs were suggestive of acute cerebellar/brainstem dysfunction. On imaging, three children demonstrated a stroke in the distribution of the posterior inferior cerebellar artery. The remaining fourth child had a "stroke-like" picture with scattered white matter lesions and a multifocal vasculitis with prominent basilar artery involvement… Data from the literature concerning eight patients gave similar results, with prominent posterior circulation stroke, multifocal vasculitis and abnormal CSF as distinctive features."*
  Pediatric stroke related to Lyme neuroborreliosis: Data from the Swiss NeuroPaediatric Stroke Registry and literature review. Monteventi O, et al. Eur J Paediatr Neurol. 2018 Jan;22(1):113-121. doi: 10.1016/j.ejpn.2017.10.010. https://pubmed.ncbi.nlm.nih.gov/29208342/, https://serval.unil.ch/en/notice/serval:BIB_89CCBFA648F7

- **Cerebral vasculitis and intracranial multiple aneurysms in a child with Lyme neuroborreliosis.** Kortela E, et al. JMM Case Rep. 2017 Apr 21;4(4):e005090. doi: 10.1099/jmmcr.0.005090. https://pmc.ncbi.nlm.nih.gov/articles/PMC5630958/ https://www.microbiologyresearch.org/content/journal/jmmcr/10.1099/jmmcr.0.005090

(e) Lyme carditis

- *"Of 207 children with early disseminated Lyme disease, 33 (16%) had carditis, 14 (42%) of whom had advanced heart block, including 9 (27%) with complete heart block… Four (12%) of 33 patients with carditis had depressed ventricular systolic function, 3 (9%) of whom required mechanical ventilation, temporary pacing, and inotropic support… The spectrum of presentation for children with Lyme carditis is broad, ranging from asymptomatic, first-degree heart block to fulminant myocarditis. Variable degrees of heart block are the most common manifestation and occasionally require temporary pacing. Transient myocardial dysfunction, although less common, can be life-threatening."*
  Lyme carditis in children: presentation, predictive factors, and clinical course. Costello JM, et al. Pediatrics. 2009 May;123(5):e835-41. doi: 10.1542/peds.2008-3058.

https://pediatrics.aappublications.org/content/123/5/e835,
https://pubmed.ncbi.nlm.nih.gov/19403477/,
https://renaissance.stonybrookmedicine.edu/sites/default/files/Lyme-carditis-Pediatrics.pdf

Sudden cardiac death secondary to Lyme carditis in paediatrics and adults (pathophysiology)

- *"We describe a case of a 17-year-old adolescent who died unexpectedly after a 3-week viral-like syndrome. Post-mortem examination was remarkable for diffuse pan-carditis characterized by extensive infiltrates of lymphocytes and focal interstitial fibrosis. In the cardiac tissue, Borrelia burgdorferi was identified via special stains, immunohistochemistry, and polymerase chain reaction. The findings support B. burgdorferi as the causative agent for his fulminant carditis and that the patient suffered fatal Lyme carditis."*
  Lyme disease: a case report of a 17-year-old male with fatal Lyme carditis. Yoon EC, et al. Cardiovasc Pathol. 2015 Sep-Oct;24(5):317-21. doi: 10.1016/j.carpath.2015.03.003. https://www.sciencedirect.com/science/article/abs/pii/S1054880715000253

a) **Cardiac Tropism of Borrelia burgdorferi: An Autopsy Study of Sudden Cardiac Death Associated with Lyme Carditis.** Am J Pathol. Muehlenbachs A, et al. 2016 May;186(5):1195-205. doi: 10.1016/j.ajpath.2015.12.027. PMID: 26968341. https://www.sciencedirect.com/science/article/pii/S0002944016000997

- **Three Sudden Cardiac Deaths Associated with Lyme Carditis** — United States, November 2012–July 2013, Morbidity and Mortality Weekly Report (*MMWR*), **December 13, 2013 / 62(49);993-996**. https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6249a1.htm

(f) Lyme arthritis

Lyme arthritis: It's never too late for joint decision making - ScienceDirecthttps://www.sciencedirect.com/science/article/pii/S2590170224000669
"Lyme arthritis should be considered in the differential of an acutely swollen large joint, especially if there has been travel to a highly endemic area (e.g., USA), even if this was several years ago or without a history of the characteristic EM rash."

(g) Ocular manifestations

Lesser RL. **Ocular manifestations of Lyme disease.** Am J Med. 1995 Apr 24;98(4A):60S-62S. doi: 10.1016/s0002-9343(99)80045x. https://pubmed.ncbi.nlm.nih.gov/7726193/
https://www.amjmed.com/article/S0002-9343(99)80045-X/abstract

Mikkilä HO, Seppälä IJ, Viljanen MK, Peltomaa MP, Karma A. **The expanding clinical spectrum of ocular Lyme borreliosis.** Ophthalmology. 2000 Mar;107(3):581-7. doi: 10.1016/s0161-6420(99)00128-1

(h) Persistent symptoms

Aucott J, Yang T, Yoon I et al. **Risk of post-treatment Lyme disease in patients with ideally-treated early Lyme disease**: A prospective cohort study. International Journal of Infectious Diseases. March 2022; 116:230-237
https://www.sciencedirect.com/science/article/pii/S1201971222000352

Delong AK, Blossom B, Maloney EL et al. **Antibiotic retreatment of Lyme disease in patients with persistent symptoms: a biostatistical review of randomized, placebo-controlled, clinical trials.** Contemp Clin Trials. 2012 Nov;33(6):1132-42
https://pubmed.ncbi.nlm.nih.gov/22922244/

Embers ME, Barthold SW, Borda JT et al. **Persistence of Borrelia burgdorferi in rhesus macaques following antibiotic treatment of disseminated infection**. PLoS One. 2012;7(1):e29914 https://pmc.ncbi.nlm.nih.gov/articles/PMC3256191/

Fallon BA, Petkova E, Keilp JG, Britton CB. **A reappraisal of the US Clinical trials of post-treatment Lyme disease syndrome.** Open Neurol J. 2012;6:79-87 https://pmc.ncbi.nlm.nih.gov/articles/PMC3474942/

Rebman AW, Aucott JN. **Post-treatment Lyme Disease as a Model for Persistent Symptoms in Lyme Disease.** Front Med (Lausanne). 2020 Feb 25;7:57
https://pubmed.ncbi.nlm.nih.gov/32161761/

Fallon BA et al **Recent Progress in Lyme Disease and Remaining Challenges.** Front Med (Lausanne). 2021 Aug 18;8:666554. doi: 10.3389/fmed.2021.666554. PMID: 34485323; PMCID: PMC8416313. https://pubmed.ncbi.nlm.nih.gov/34485323/
"..mounting evidence supports the idea that a substantial number of patients experience persistent symptoms following treatment. The research community has largely lacked the necessary funding to properly advance the scientific and clinical understanding of the disease, or to develop and evaluate innovative approaches for prevention, diagnosis, and treatment….This review article summarizes progress over the past 5 years in our understanding of Lyme and tick-borne diseases in the United States and highlights remaining challenges."

5. Lyme disease in pregnancy

NICE guideline on Lyme disease: *"The committee acknowledged that mother-to-baby transmission of Lyme disease is possible in theory."* **Rationale-and-impact/Lyme disease/Guidance/NICE**

NICE reviewed congenital transmission through a limited set of observational studies
Person To Person-transmission Lyme disease/Evidence/ Nice

CDC guidance in 2024 states:
"Untreated Lyme disease during pregnancy can lead to infection of the placenta. Spread from mother to fetus is possible but rare"
"There are no published studies assessing developmental outcomes of children whose mothers acquired Lyme disease during pregnancy."

A systematic review on the impact of gestational Lyme disease in humans on the fetus and newborn Waddell et al. PLoSOne 2018 Nov 12;13(11):e0207067. Doi: 10.1371/journal.pone.0207067 https://pubmed.ncbi.nlm.nih.gov/30419059/

An Overview of Tickborne Infections in Pregnancy and Outcomes in the Newborn: The Need for Prospective Studies Frontiers in Medicine Lambert https://www.frontiersin.org/journals/medicine/articles/10.3389/fmed.2020.00072/full

6. Lyme Disease Research Centres

Johns Hopkins Lyme Disease Research Center
Johns Hopkins Medicine Lyme Disease Research Centre is pioneering multidisciplinary research in all manifestations of Lyme disease, with a mission to improve patient care.

Columbia University - Lyme & Tick-Borne Diseases Research Center
https://www.columbia-lyme.org/
The Lyme and Tick-borne Diseases Research Center was established as the first academic research centre in USA to focus multidisciplinary research on chronic Lyme disease.

Bay Area Lyme Foundation
Bay Area Lyme Foundation is a national, non-profit organization based in Silicon Valley and collaborates with world-class scientists and institutions to accelerate medical breakthroughs for Lyme disease.

7. Lyme Resource Centre

Lyme Resource Centre - Scottish Registered charity (SC049151) with a mission to minimise risk of Lyme disease whilst enjoying the outdoors, by educating the public and health professionals about ticks and Lyme disease.

By working both independently and in partnerships we are:

- Educating the public through a variety of methods and outreach activities
- Providing educational resources for health professionals
- Supporting patients by signposting to accredited sources of information
- Working with others in the medical, veterinary and scientific communities to address the genuine scientific uncertainties in relation to all aspects of diagnosis and treatment

Contact - admin@lymeresourcecentre.com

LRC - Lyme disease awareness for under 12yr olds - children's animation

LRC Lyme disease Experience Survey https://www.lymeresourcecentre.com/experience-survey

https://www.lymeresourcecentre.com/_files/ugd/f8e714_21e842fc9c0f4d1a824cc77cc82926a7.pdf

https://www.facebook.com/lymeresourcecentrescotland

https://www.instagram.com/lymeresourcecentre/

https://x.com/LymeResourceCtr

https://www.linkedin.com/company/28960771

Lyme Resource Centre - YouTube