Clinical assessment

Diagnose Lyme disease in people with erythema migrans, defined as a red rash that:
- increases in size and may sometimes have a central clearing,
- is not usually itchy, hot or painful,
- usually becomes visible from 1 to 4 weeks (but can appear from 3 days to 3 months) after a tick bite and lasts for several weeks,

Diagnosis

- is usually at the site of a tick bite.
- See NICE visual images: Lyme disease: erythema migrans.
- Be aware that a rash, which is not erythema migrans, can develop as a reaction to a tick bite that:
  - usually develops and recedes during 48 hours from the time of the tick bite,
  - is more likely than erythema migrans to be hot, itchy or painful,
  - may be caused by an inflammatory reaction or infection with a common skin pathogen.
- Consider the possibility of Lyme disease in people presenting with several of the following symptoms, because Lyme disease is a possible but uncommon cause of:
  - fever and sweats, swollen glands, malaise, fatigue, neck pain or stiffness, migratory joint or muscle aches and pain, cognitive impairment, such as memory problems and difficulty concentrating, headache, paraesthesias.

Raising awareness of Lyme disease

- Be aware that:
  - bacteria that cause Lyme disease are transmitted by the bite of an infected tick,
  - ticks are mainly found in grassy and wooded areas, including urban gardens and parks,
  - tick bites may not always be noticed,
  - infected ticks are found throughout the UK and Ireland, and although some areas appear to have a higher prevalence of infected ticks, prevalence data are incomplete,
  - particularly high-risk areas are the South of England and Scottish Highlands but infection can occur in many areas,
  - Lyme disease may be more prevalent in parts of central, eastern and northern Europe (including Scandinavia) and parts of Asia, the US and Canada,
  - most tick bites do not transmit Lyme disease and prompt, correct removal of the tick reduces the risk of transmission.
- Give people advice about:
  - where ticks are commonly found,
  - the importance of prompt, correct tick removal and how to do this (see Public Health England's leaflet Enjoy the outdoors but be 'tick aware'),
  - covering exposed skin and using insect repellents that protect against ticks,
  - how to check themselves and their children for ticks on the skin,
  - sources of information on Lyme disease, such as Public Health England, and patient charities.

Definition of terms

<table>
<thead>
<tr>
<th>IR</th>
<th>immediate release</th>
</tr>
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<tbody>
<tr>
<td>IV</td>
<td>intravenous</td>
</tr>
<tr>
<td>PNS</td>
<td>peripheral nervous system</td>
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<tr>
<td>CNS</td>
<td>central nervous system</td>
</tr>
</tbody>
</table>

Background

- Lyme disease (Lyme borreliosis) is a tick-borne infectious disease. It is caused by different genospecies of Borrelia including B. burgdorferi sensu strictu, B. afzelii and B. garinii, which can be transmitted to humans through a bite from an infected tick. Infection is more likely the longer a tick is attached to the skin.
- Raising awareness of Lyme disease

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Diagnosis

- Diagnose Lyme disease in people with erythema migrans, defined as a red rash that:
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**Laboratory investigations**
- See NICE visual summary for recommendations on laboratory testing.
- Diagnose and treat Lyme disease without laboratory testing in people with erythema migrans.
- Use a combination of clinical presentation and laboratory testing to guide diagnosis and treatment in people without erythema migrans. Do not rule out diagnosis if tests are negative but there is high clinical suspicion of Lyme disease.
- Carry out tests for Lyme disease only at laboratories that:
  - are accredited by the UK accreditation service (UKAS), **AND**
  - use validated tests (validation should include published evidence on the test methodology, its relation to Lyme disease and independent reports of performance), **AND**
  - participate in a formal external quality assurance programme.
- Do **NOT** routinely diagnose Lyme disease based only on tests done outside the NHS, unless the laboratory used is accredited, participates in formal external quality assurance programmes and uses validated tests. If there is any doubt about tests:
  - review the person’s clinical presentation, **AND**
  - carry out testing again using a UKAS-accredited laboratory and/or seek advice from a national reference laboratory.

**Information for people being tested for Lyme disease**
- Tell people that tests for Lyme disease have limitations. Explain that both false-positive and false-negative results can occur and what this means.
- Explain to people that most tests for Lyme disease assess for the presence of antibodies, and that the accuracy of tests may be reduced if:
  - testing is carried out too early (before antibodies have developed),
  - the person has reduced immunity e.g. people on immunosuppressant treatments, which might affect the development of antibodies.
- Advise people that tests from non-UKAS laboratories may not have been fully evaluated to diagnose Lyme disease.
- Explain to people that:
  - the symptoms and signs associated with Lyme disease overlap with those of other conditions,
  - they will be assessed for alternative diagnoses if their tests are negative and their symptoms have not resolved,
  - symptoms such as tiredness, headache and muscle pain are common and a specific medical cause is often not found.

**Treatment and management**
- For adults and young people (≥12 years) offer antibiotic treatment according to their symptoms as described in **Table 1**.
- For children (<12 years) offer antibiotic treatment according to their symptoms as described in **Table 2**.
- Ask women (including young women <18 years) if they might be pregnant before offering antibiotic treatment.
- For pregnant women:
  - treat Lyme disease using appropriate antibiotics for the stage of pregnancy,
  - start treatment for Lyme disease under specialist care for babies of women treated for Lyme disease during pregnancy if the baby has IgM antibodies specific for Lyme disease or there is any suspicion the baby may be infected.
- If symptoms worsen during treatment, assess for an allergic reaction to the antibiotic. Be aware that a Jarisch-Herxheimer reaction (see **Box 1**) may cause an exacerbation of symptoms but does not usually warrant stopping treatment.
- Consider clinical review during or after treatment to assess for possible side effects and response to treatment.

**Box 1**
- Jarisch-Herxheimer reaction
  - This is a systemic reaction, thought to be caused by the release of cytokines when antibiotics kill large numbers of bacteria.
  - Symptoms include a worsening of fever, chills, muscle pains, and headache.
  - The reaction can start between 1 and 12 hours after antibiotics are started but can also occur later and can last for a few hours or 1 or 2 days. The reaction is self-limiting and usually resolves within 24 to 48 hours.
  - Inform people to contact their doctor and keep taking their antibiotics if symptoms worsen.

**Emergency referral**
- Follow usual clinical practice for emergency referrals, e.g. in people with symptoms that suggest CNS infection, uveitis or cardiac complications such as complete heart block, even if Lyme disease is suspected.

**Information and advice**
- Explain to people diagnosed with Lyme disease that:
  - it is a bacterial infection treated with antibiotics,
  - most people recover completely,
  - prompt antibiotic treatment reduces the risk of further symptoms developing and increases the chance of complete recovery,
  - it may take time to get better, but their symptoms should continue to improve in the months after antibiotic treatment,
  - some people treated with antibiotics may have a Jarisch-Herxheimer reaction to treatment (see **Box 1**),
  - they may need additional treatment for symptom relief,
  - infection does not give lifelong immunity and that it is possible to be re-infected and develop Lyme disease again,
  - if symptoms have not improved or return after completing treatment they should speak to their doctor.
- For pregnant women, also:
  - tell them that they are unlikely to pass the infection to their baby and emphasise the importance of completing the full course of antibiotic treatment,
  - advise women who had Lyme disease during pregnancy to let their healthcare professional know if they have any concerns about their baby. In this situation, healthcare professionals should discuss the history with a paediatric infectious disease specialist and seek advice on what investigations to perform.

**Specialist advice**
- If an adult with Lyme disease has focal symptoms, consider a discussion with or referral to an appropriate specialist e.g. an adult infection specialist, rheumatologist or neurologist.
- Discuss the diagnosis and management of Lyme disease in children and young people under 18 years with an appropriate specialist, unless they have a single erythema migrans lesion and no other symptoms e.g. a paediatrician, paediatric infectious disease specialist or a paediatric neurologist.

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**Please go to** [www.nice.org.uk](http://www.nice.org.uk) **to check for any recent updates to this guideline.**
**Ongoing symptoms after a course of antibiotics**

- If symptoms that may be related to Lyme disease persist, do not continue to improve or worsen after treatment, review the person’s history and symptoms to explore:
  - possible alternative causes of the symptoms,
  - if re-infection may have occurred,
  - if treatment may have failed,
  - details of any previous treatment, including whether the course of antibiotics was completed without interruption,
  - if symptoms may be related to organ damage caused by Lyme disease, e.g. nerve palsy.

- If the person’s history suggests re-infection, offer antibiotic treatment for Lyme disease according to their symptoms (see Table 1 for adults and young people ≥12 years and Table 2 for children <12 years).

- Consider a second course of antibiotics for people with ongoing symptoms if treatment may have failed. Use an alternative antibiotic to the initial course.

- If a person has ongoing symptoms following two completed courses of antibiotics for Lyme disease:
  - do not routinely offer further antibiotics, AND
  - consider discussion with a national reference laboratory or discussion or referral to a specialist.

**Non-antibiotic management of ongoing symptoms**

- Offer regular clinical review and reassessment to people with ongoing symptoms, including people who have no confirmed diagnosis.

- Explore any ongoing symptoms with the person and offer additional treatment if needed following usual clinical practice.

- Be alert to the possibility of symptoms related to Lyme disease that may need assessment and management, including:
  - chronic pain,
  - depression and anxiety,
  - fatigue.

**Table 1. Antibiotic treatment in adults and young people (≥12 years) according to symptoms**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>First-line treatment</th>
<th>Second-line treatment</th>
<th>Third-line treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythema migrans and/or non-focal symptoms</td>
<td><strong>Oral doxycycline</strong>: 100mg twice per day OR 200mg once per day for 21 days</td>
<td><strong>Oral amoxicillin</strong>: 1g three times per day for 21 days</td>
<td><strong>Oral azithromycin</strong>: 500mg once per day for 17 days</td>
</tr>
<tr>
<td><strong>Lyme disease without focal symptoms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lyme disease affecting the cranial nerves or PNS</td>
<td><strong>Oral doxycycline</strong>: 100mg twice per day OR 200mg once per day for 21 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lyme disease affecting the CNS</td>
<td><strong>IV ceftriaxone</strong>: 2g twice per day OR 4g once per day for 21 days</td>
<td><strong>Oral doxycycline</strong>: 200mg twice per day OR 400mg once per day for 21 days</td>
<td></td>
</tr>
<tr>
<td>Lyme disease arthritis Acrodermatitis chronica atrophicans</td>
<td><strong>Oral doxycycline</strong>: 100mg twice per day OR 200mg once per day for 28 days</td>
<td><strong>Oral amoxicillin</strong>: 1g 3 times per day for 28 days</td>
<td><strong>IV ceftriaxone</strong>: 2g once per day for 28 days</td>
</tr>
<tr>
<td>Lyme carditis</td>
<td><strong>Oral doxycycline</strong>: 100mg twice per day OR 200mg once per day for 21 days</td>
<td></td>
<td><strong>IV ceftriaxone</strong>: 2g once per day for 21 days</td>
</tr>
<tr>
<td>Lyme carditis and haemodynamically unstable</td>
<td><strong>IV ceftriaxone</strong>: 2g once per day for 21 days</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**Resources**

NICE visual images: Lyme disease: erythema migrans.

NICE visual summary: Lyme disease: laboratory investigations and diagnosis

Public Health England

Lyme disease: resources and guidance

Tick bite risks and prevention of Lyme disease

Lyme Disease UK

www.lymediseaseuk.com/lyme-disease/

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This bulletin summarises key prescribing points from NICE guidance. Please refer to the full guidance at www.nice.org.uk for further detail. This is an NHS document not to be used for commercial purposes.
Table 2. Antibiotic treatment in children (<12 years) according to symptoms

- Discuss management of Lyme disease in children and young people with a specialist, unless they have a single erythema migrans lesion with no other symptoms.
- Children weighing more than the amounts specified should be treated according to Table 1.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Age</th>
<th>First-line treatment</th>
<th>Second-line treatment</th>
<th>Third-line treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythema migrans and/or non-focal symptoms</td>
<td>9 to 12 years</td>
<td>Weight &lt;45kg: oral doxycycline IR U* 5mg/kg in 2 divided doses on day 1 followed by 2.5mg/kg daily in 1 or 2 divided doses for a total of 21 days For severe infections, up to 5mg/kg daily for 21 days</td>
<td>Weight ≤33kg: oral amoxicillin 30mg/kg 3 times per day for 21 days</td>
<td>Weight ≤50kg: oral azithromycin U* 10mg/kg daily for 17 days</td>
</tr>
<tr>
<td></td>
<td>&lt;9 years</td>
<td>Weight ≤33kg: oral amoxicillin 30mg/kg 3 times per day for 21 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lyme disease affecting the cranial nerves or PNS</td>
<td>9 to 12 years</td>
<td>Weight &lt;45kg: oral doxycycline IR U* 5mg/kg in 2 divided doses on day 1 followed by 2.5mg/kg daily in 1 or 2 divided doses for a total of 21 days For severe infections, up to 5mg/kg daily for 21 days</td>
<td>Weight ≤33kg: oral amoxicillin 30mg/kg 3 times per day for 21 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;9 years</td>
<td>Weight ≤33kg: oral amoxicillin 30mg/kg 3 times per day for 21 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lyme disease affecting the CNS</td>
<td>9 to 12 years</td>
<td>Weight ≤50kg: IV ceftriaxone 80mg/kg once per day for 21 days</td>
<td>Weight &lt;45kg: oral doxycycline IR U* 5mg/kg in 2 divided doses on day 1 followed by 2.5mg/kg daily in 1 or 2 divided doses for a total of 21 days For severe infections, up to 5mg/kg daily for 21 days</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Lyme disease arthritis or acrodermatitis chronica atrophicans</td>
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<tr>
<td></td>
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<td>Weight ≤33kg: oral amoxicillin 30mg/kg 3 times per day for 28 days</td>
<td></td>
<td>Weight ≤50kg: IV ceftriaxone 80mg/kg once per day for 28 days</td>
</tr>
<tr>
<td>Lyme carditis (both haemodynamically stable and unstable)</td>
<td>9 to 12 years</td>
<td>Weight &lt;45kg: oral doxycycline IR U* 5mg/kg in 2 divided doses on day 1 followed by 2.5mg/kg daily in 1 or 2 divided doses for a total of 21 days For severe infections, up to 5mg/kg daily for 21 days</td>
<td>Weight ≤50kg: IV ceftriaxone 80mg/kg once per day for 21 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;9 years</td>
<td>Weight ≤50kg: IV ceftriaxone 80mg/kg once per day for 21 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a doxycycline is contraindicated in children under 12 years. The use of doxycycline for children aged ≥9 years in infections where doxycycline is considered first line in adult practice is accepted specialist practice. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Obtain and document informed consent. b Do NOT use azithromycin to treat people with cardiac abnormalities associated with Lyme disease because of its effect on QT interval. U unlicensed indication. Obtain and document informed consent.</td>
<td></td>
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<td></td>
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</tr>
</tbody>
</table>

**Recommendations** – wording used such as ‘offer’ and ‘consider’ denote the strength of the recommendation.

**Drug recommendations** – the guideline assumes that prescribers will use a drug’s Summary of Product Characteristics (SPC) to inform treatment decisions.

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