


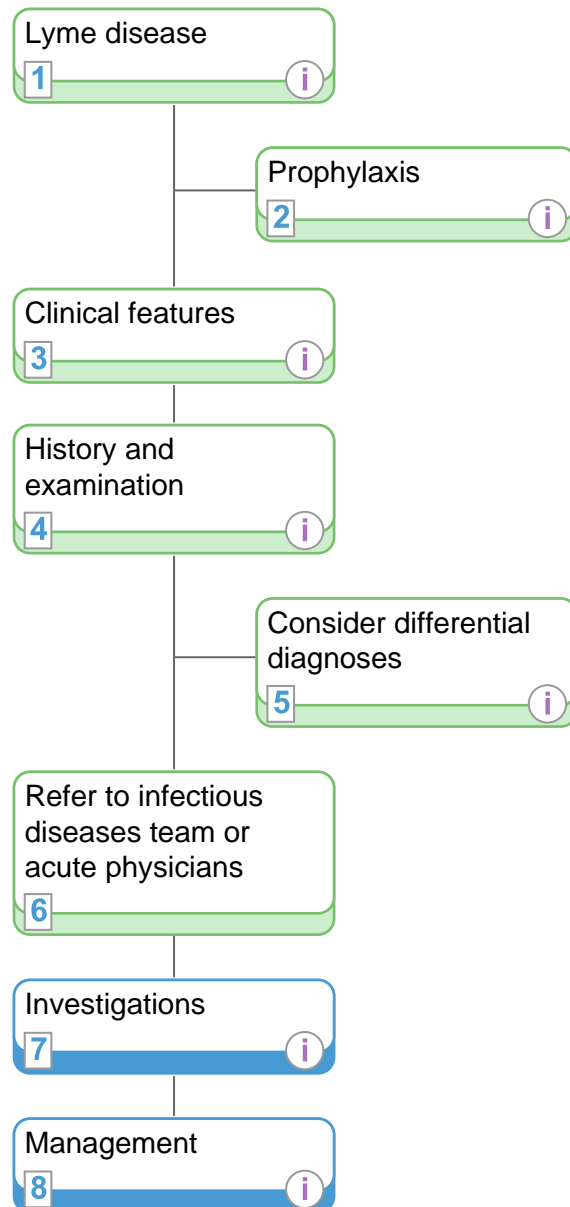


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 Information
 Primary care
 Secondary care



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Lyme disease

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1 Lyme disease

Quick info:

Scope:

- diagnosis and management of Lyme disease (otherwise known as Lyme borreliosis)

Pathogenesis:

- disease is caused by the tick-borne spirochaete *Borrelia burgdorferi* (*B. burgdorferi*)
- co-infection with other organisms that share the same tick vector may also be present, including:
 - anaplasma
 - ehrlichia
- there are 4 pathogenic groups:
 - *B. burgdorferi* (North American)
 - *B. garinii* (Europe)
 - *B. afzelii* (Europe)
 - *B. spielmani* (Europe)
- ticks become active in the spring but illness can begin at any time of the year (stage 1)
- may be asymptomatic
- may begin with the characteristic skin rash, erythema migrans, in 35-60% of cases and, over a course of two weeks, spread to other sites (stage 2), including:
 - synovial fluid
 - connective tissue
 - nervous system
 - heart and joints
- it becomes a persistent infection over months or years (often after a latent period)
- can remain sequestered in:
 - connective tissue
 - synovium
 - central nervous system (CNS)
- there may be down regulation or modification of surface antigens to evade the body's immune system

Incidence and prevalence:

- endemic areas are temperate regions of North America, Europe and Asia
- incidence of Lyme disease in the UK is not well documented but there are an estimated 1,600-2,600 cases of Lyme disease annually:
 - of the 600 confirmed cases in 2005, 500 cases were acquired in the UK and 100 abroad
- 80-12,000 cases in Europe annually
- 20,000 cases in US annually

Risk factors:

- travel to endemic area
- tick bites and inadequate tick prevention
- more common during summer season to coincide with tick activity but cases are reported throughout the year

Mode of transmission:

- Lyme disease is transmitted to humans by the bite of a hard-bodied tick carrying the spirochaete *B. burgdorferi*
- ticks have a 3 stage life cycle:
 - larva
 - nymph (infectious)
 - adult (infectious)

Incubation period:

- usually 7-10 days following tick exposure for early localised disease
- the incubation period for other phases is longer

Notification:

- Lyme disease is not a notifiable disease in the UK, however microbiology laboratories voluntarily report confirmed cases

Controversies:

- Lyme disease management remains controversial at present as there are two distinct schools of thought regarding disease epidemiology and treatment duration
- the Infectious Diseases Society of America (IDSA) maintains that Lyme disease is:
 - rare
 - confined to well described geographical locations
 - easy to diagnose
 - easy to cure

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- the International Lyme and Associated Diseases Society (ILADS) contradicts the IDSA and states that Lyme disease is:
 - much more common than previously believed
 - less well geographically confined
 - harder to diagnose than previously though
 - harder to cure than previously thought
- the IDSA guidelines are currently more widely accepted (eg by the Centres for Disease Control and Prevention [CDC]) than the ILADS guidelines but there is much ongoing controversy
- there is current evidence to support both IDSA and ILADS schools of thought and it may be some time until one set of guidelines becomes generally more accepted than the other

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2 Prophylaxis

Quick info:

Advise patients travelling to endemic areas on:

- prevention of tick bites, including:
 - keeping skin covered
 - use of tick repellent:
 - permethrin on clothes
 - DEET on skin
 - examine clothes and exposed skin for ticks every 3-4 hours and also after returning home
- removal of a tick:
 - aim to remove immediately as transmission increases after 24 hours of attachment
 - gloves should be used when removing a tick
 - ticks should not be covered with oily substances such as petroleum jelly as these could enhance transmission of the Lyme spirochaete
 - do not use lighted cigarettes or glowing match heads
 - an attached tick should be grasped with fine tweezers or a tick remover as close to the skin as possible and pulled away with steady traction until the tick releases from the skin
- routine use of antibiotic prophylaxis for the prevention of Lyme disease remains unclear, although short courses have been used in prophylaxis after tick bite during pregnancy:
 - prophylactic antibiotics after tick bites in Lyme disease endemic areas have been shown to be beneficial
- there is currently no vaccine available – a vaccine available in the United States was withdrawn in 2002

People who live in endemic areas can consider landscape modification or other methods of environmental control around their home.

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3 Clinical features

Quick info:

Clinical features are divided into 3 stages:

- stage 1 (early localised borreliosis):

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Lyme disease

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- classical erythema migrans rash
- limited pyrexia and local lymphadenopathy
- rarely borrelial lymphocytoma
- stage 2 (early disseminated Lyme borreliosis):
 - occurs weeks to months after initial infection
 - spirochaetes spread to more distant sites via bloodstream and lymph system
 - flu-like illness
 - sweats
 - myalgia
 - conditions of the:
 - skin
 - nervous system
 - heart
 - joints
- stage 3 (late borreliosis):
 - acrodermatitis chronica atrophicans accompanying myalgia
 - mild to moderate sensory neuropathy
 - chronic oligoarthritis (thought to be rare but may be under reported)
 - disease may not progress to later stages
 - patients may occasionally present with symptoms and signs of later disease without recalling earlier disease features
 - persistent symptoms and long-term fatigue associated with Lyme disease is sometimes called post-Lyme syndrome

Lyme disease in pregnancy can cause stillbirth or neonatal death.

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Health Protection Agency (HPA). Zoonoses: Lyme borreliosis: Epidemiology; 2006.

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4 History and examination

Quick info:

Ask about risk factors:

- recent or previous travel to endemic area
- lack of use of tick barriers (clothing to cover skin, use of insect repellent)
- history of tick bite
- diagnosed Lyme or other illnesses in pets

Ask about and examine for typical features of the different stages:

- stage 1 (early localised Lyme borreliosis):
 - classical erythema migrans rash:
 - erythema migrates out from site of tick bite
 - previously affected skin returns to normal as rash advances
 - areas of rash of 70cm diameter have been reported
 - rash more apparent after bath or heavy exercise
 - limited pyrexia
 - local lymphadenopathy
 - borrelial lymphocytoma (blue-red nodule or plaque) can last a few months to over a year if left untreated – it is more common in children (on earlobe) and rarer in adults (on nipple)
- stage 2 (early disseminated Lyme borreliosis):
 - a combination of the following may occur:
 - flu-like illness
 - sweats
 - myalgia
 - multiple areas of erythema migrans
 - isolated facial palsy – can be bilateral
 - other facial and cranial nerve palsies
 - meningitis symptoms
 - peripheral neuritis – resembling mononeuritis multiplex

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- sensory radiculitis – paraesthesia in areas of affected spinal nerve roots
- mixed sensorimotor radiculitis
- arthralgia (especially small joints)
- flitting inflammatory arthritis – few patients progress to chronic arthritis (most commonly seen in North America)
- cardiac conduction disturbances – mainly heart blocks, often of short duration
- cardiomyopathy (rare)
- carditis (rare)
- hepatitis
- orchitis
- anterior and posterior uveitis
- panophthalmitis
- stage 3 (late Lyme borreliosis):
 - acrodermatitis chronica atrophicans – blue-red discolouration of skin and subsequent epidermal atrophy
 - accompanying mild to moderate sensory neuropathy
 - signs of chronic oligoarthritis (swelling, tenderness)
 - Lyme encephalopathy:
 - the true incidence is unknown but it may be up to 70% in cases with late disease
 - may result in long-term impaired mental test score (memory), spastic paraparesis, sensory polyneuropathy

References:

- Health Protection Agency (HPA). Zoonoses: Lyme borreliosis: Epidemiology. 2006.
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- Brouqui P, Bacellar F, Baranton, G et al. Guidelines for the diagnosis of tick-borne bacterial diseases in Europe. *Clin Microbiol & Infect* 2004; 10: 1108-32.

5 Consider differential diagnoses

Quick info:

The differential diagnosis depends on the suspected stage of Lyme infection:

- stage 1 (early localised Lyme borreliosis):
 - erythema annulare
 - annular tinea infection
 - fixed drug eruption
 - reaction to insect bite
 - co-infection with anaplasma or ehrlichia
- stage 2 (early disseminated Lyme borreliosis):
 - vasculitis
- stage 3 (late Lyme borreliosis):
 - chronic fatigue syndrome (CFS)
 - venous insufficiency
 - causes of Bell's palsy
 - causes of cardiac conduction defects

Reference:

- Steere A. Medical Progress: Lyme disease. *N Engl J Med* 2001; 345: 115-25.
- O'Connell S. Fortnightly review: Lyme disease in the United Kingdom. *BMJ* 1995; 310: 303-8.

7 Investigations

Quick info:

The diagnosis is primarily based on clinical observation and history of exposure to ticks in patients with a classic erythema migrans rash.

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In patients without a classical clinical picture there are several diagnostic tests in use:

- antibody detection to *Borrelia burgdorferi* (*B. burgdorferi*; gold standard)
- enzyme-linked immunosorbent assay (ELISA)
- immunoblotting technique:
 - is used to confirm the ELISA
 - has a combined specificity with ELISA of 99% but a poor sensitivity of 56%
 - the two-tiered system of ELISA and immunoblotting is more rapid than other diagnostic methods but the poor combined sensitivity means that better tests are needed
 - there may be cross reactions with rheumatoid factor, antinuclear antibodies and infectious mononucleosis and may also provide false positive results with other borrelia, *Treponema pallidum* and oral spirochaetes if immunoblotting is used alone
- microbiological culture (low yield and takes 3-4 weeks)
- DNA detection using polymerase chain reaction (PCR) – valuable in atypical presentations but has a problem with false positive and false negative results
- cerebrospinal fluid (CSF) analysis revealing:
 - lymphocytosis
 - normal glucose
 - mildly elevated protein
 - culture low yield
 - borrelial DNA PCR
- association of arthritis with HLA – DRB1 alleles

References:

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8 Management

Quick info:

Antibiotics are the generic treatment and current guidelines from the the Infectious Diseases Society of America (IDSA) are as follows:

- erythema migrans:
 - amoxicillin orally for 14-21 days; or
 - doxycycline orally for 10-21 days – doxycycline should not be used in children under age 8 years or pregnant women; or
 - cephalosporin – if amoxicillin or doxycycline are contraindicated
- macrolides:
 - erythromycin or azithromycin are not currently recommended as first-line therapy for treating any stage of Lyme borreliosis due to high failure rate
 - if macrolides are given (eg if multiple allergies to other drugs) then patients should be monitored closely for treatment failure
- borrelial lymphocytoma or acrodermatitis chronica atrophicans:
 - as for erythema migrans but for 21-30 days
- isolated facial palsy:
 - as for erythema migrans but for 21-30 days
 - ensure no other central nervous system (CNS) involvement – if in doubt, treat as other CNS manifestations
- other CNS manifestations:
 - intravenous (IV) cefotaxime for 14 days; or
 - doxycycline orally for 21 days and IV ceftriaxone 14-21 days
- carditis:
 - as for erythema migrans but for 21 days; or
 - cefotaxime for 14 days or ceftriaxone for 14-21 days – if severe carditis
- arthritis:
 - amoxicillin orally for 30 days; or
 - doxycycline orally for 30 days (as effective as amoxicillin plus probenecid); or
 - IV ceftriaxone for 14-21 days
 - cefotaxime and ceftriaxone are both more effective than penicillin
 - penicillin (more effective than placebo)

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- for late Lyme disease:
 - cefotaxime is likely to be beneficial
 - it is not known whether ceftriaxone is beneficial when given alone
 - ceftriaxone in combination with doxycycline is not effective

In general:

- long-term antibiotic therapy in patients with persistent symptoms is thought to provide no additional benefit
- monitor response based on clinical improvement
- beware of potential adverse drug reactions
- Jarisch-Herxheimer reactions may occur shortly after start of treatment
- patients should have daily electrocardiograms (ECGs) during admission to detect evidence of cardiac conduction defects

The alternative view by the International Lyme and Associated Diseases Society (ILADS) is:

- treatment with antibiotics is needed for a longer duration than is currently common practice, especially in patients with continuing symptoms (post-Lyme syndrome)
- some studies have shown that longer courses of antibiotics (eg one month of IV ceftriaxone) improve the primary outcome of fatigue in post-Lyme syndrome as well as improvements in long-term cognition and physical functioning

In the absence of current consensus between IDSA and ILADS:

- longer course (more than 21 days) of antibiotics may be beneficial in some sub-groups of patients, eg Lyme encephalopathy, post-Lyme disease, after consultation with Lyme experts

References:

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Key Dates

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Accreditations

The pathway is accredited by:

The Chief Knowledge Officer of the NHS:

Accreditation attained: 30-Apr-2008

Due for review: 29-Feb-2012

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Evidence summary for Lyme disease

The pathway is consistent with the following quality-appraised guidelines (14,18,21). All intervention nodes have been assessed for consistency with high quality guidelines and underlying evidence.

Search date: Mar-2008

Evidence grades:

- 1** Intervention node supported by level 1 guidelines or systematic reviews
- 2** Intervention node supported by level 2 guidelines
- E** Intervention node based on expert clinical opinion
- U** Non-intervention node, not graded

Evidence grading:

Graded node titles that appear on this page

Graded node titles that appear on this page	Evidence grade	Reference IDs
Lyme disease	U	14, 11, 7, 4, 6
Prophylaxis	2	14, 11, 7, 9, 15, 2, 10
Clinical features	U	14, 18, 4, 10, 11
Management	2	17, 14, 12, 11, 7, 1, 6, 13, 19, 16
History and examination	2	14, 4, 11, 20, 3, 8, 21
Consider differential diagnoses	U	7, 11
Investigations	2	14, 4, 11, 7, 5

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This is a list of all the references that have passed critical appraisal for use in the pathway Lyme disease

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