

FAQs Lyme serology, Lyme disease (aka Lyme borreliosis)

Before diagnostic tests are requested, a patient's risk of exposure to ticks should be properly assessed and the clinical history evaluated for features compatible with Lyme borreliosis.

Tests should not be requested if there is no significant risk of a patient having Lyme borreliosis.

It is important that relevant clinical information is provided when samples are submitted for testing:

- date of tick bite
- date of symptom onset
- nature of symptoms
- country in which tick bite occurred
- how long tick was attached before removal

(Samples received without such information may be stored without testing, so inclusion with the request prevents delay)

Not all ticks carry *B. burgdorferi* so a tick bite does not mean Lyme borreliosis is inevitable. It is generally thought that early tick removal reduces the risk of transmission, but as ticks may go unnoticed this is often not useful in determining risk.

We test for Lyme IgG and IgM locally, suggestive of previous or recent Lyme infection respectively, and then forward positive specimens to the Lyme disease laboratory services at Public Health England Porton for immunoblot testing.

1. Possible erythema migrans. Should I send serology?

No, not if the rash is characteristic and there is a history of tick bite. Erythema (chronicum) migrans in the UK is generally pathognomonic for Lyme disease [1]. If there is a tick exposure and a typical erythema migrans rash we would advise treatment and serology is not required to confirm the diagnosis.

Erythema migrans is a distinctive circular rash at the site of the tick bite. It usually occurs 3 to 30 days after being bitten and is often described as looking like a bull's-eye on a dart board. The affected area of skin will be red and the edges may feel slightly raised. The size of the rash can vary significantly and it may expand over several days or weeks. Typically it's around 15cm (6 inches) across, but it can be much larger or smaller than this.

Some people may develop several rashes in different parts of their body. However, around

one in every three people with Lyme disease do not report seeing a rash.



Early Lyme is serologically positive in 30-70% at presentation. Antibody response may be further delayed or abrogated in patients who have received empirical treatment. This means that both acute and convalescent serology results can be negative.

Recommended treatment in adults is doxycycline 100mg bd po for 2 weeks, or amoxicillin 500mg tds po for 2 weeks.

Oral therapy is highly effective and outcomes are excellent with 92-99% cure rate at 12-24 months [2,3].

[1] Clin Dermatol. 2006 Nov-Dec;24(6):509-20.

[2] Clinical Infectious Diseases 2010;50:512–20

[3] Clinical Infectious Diseases 2012;55(3):343–50

2. Treated for erythema migrans. Should I test Lyme serology now, post antibiotics?

No, it is not necessary. The antibody response takes several weeks to reach a detectable level, so antibody tests in the first few weeks of infection may be negative. Antibody response may be further delayed or abrogated in patients who have received empirical treatment.

3. Tick bite but no symptoms. Should I test for Lyme serology / treat empirically?

No, serology testing is not indicated, and there is no recommendation for pre-emptive treatment. If they develop Erythema migrans then they should be treated on the basis of this clinical diagnosis (see Q1 above). If any other symptoms of possible Lyme borreliosis develop, then a serum sample should be submitted 4-6 weeks after the bite with the relevant information (date of tick bite, date of symptom onset, nature of symptoms, etc) included. Early antibiotic therapy is not critical. Early testing may lead to false negative results during seroconversion.

4. Treatment of Lyme in penicillin allergic patients

Doxycycline is the first line antibiotic for oral treatment of Lyme disease. The BNF contraindicates doxycycline in children under 12 years old and pregnant or breastfeeding women. Amoxicillin is an alternative agent for oral treatment of erythema migrans in these patient groups. Cefuroxime axetil is an option for such patients with non-severe penicillin allergy. See below (Q8) for regimens.

5. I think my patient might have Lyme arthritis. What tests should I send?

If you suspect Lyme arthritis, send a serum sample for Lyme IgG with appropriate clinical details (date of symptom onset, joint affected, presence of clinical findings eg effusion, plausibility of tick exposure, likely country of tick exposure). Aspirated joint fluid should also be considered for Lyme PCR.

Lyme arthritis usually affects the knee, with synovitis, effusion and pain. Effusion is commonly a striking presenting feature, out of proportion to the degree of pain experienced. Patients have usually had earlier intermittent episodes of arthritis before the condition becomes persistent. Lyme arthritis is particularly associated with infections acquired in the USA and in some focal areas of Europe as it occurs mainly in patients with *B. burgdorferi* sensu stricto infections. The condition has become less common in recent years because of better recognition and treatment of Lyme borreliosis at earlier stages of infection.

Treatment of Lyme arthritis is with doxycycline or amoxicillin for 28 days. If this fails, then intravenous ceftriaxone should be considered. Non steroidal anti-inflammatory drugs may be used during initial treatment.

Intra-articular steroid injections are not recommended unless there is a post-treatment persistence of joint inflammation and synovial fluid and/or synovium biopsies are negative for borrelial DNA in PCR tests. Such persistence, which is termed antibiotic-refractory Lyme arthritis and is thought to have an autoimmune component, should be managed by a rheumatologist. Arthroscopic synovectomy may improve persistent synovitis but is rarely required.

6. My patient has symptoms of fatigue and is worried about chronic Lyme disease. What tests should I send?

Fatigue, without any other features consistent with Lyme borreliosis, would not be an indication for testing. This is because a positive Lyme IgG result may indicate past Lyme borreliosis but does not indicate that the current fatigue is due to ongoing infection.

It is necessary to carefully review the history of any patient presenting with fatigue and a concern about chronic Lyme disease. Are there any features of previous Lyme borreliosis (definite tick bite, erythema migrans, symptoms suggestive of early Lyme disease)? Are there any features suggestive of current late Lyme borreliosis (arthritis, chronic encephalomyelitis, radiculopathy, carditis, acrodermatitis chronica atrophicans)?

Acrodermatitis chronica atrophicans (ACA) is an uncommon late cutaneous manifestation causing longstanding bluish-red lesions usually on extensor surfaces of limbs, which may become atrophic and can be accompanied by a peripheral neuropathy. It usually affects older adults, predominantly women.



A small proportion of patients have persistent subjective symptoms following apparently appropriate treatments for Lyme borreliosis, and without new clinical signs or laboratory evidence of ongoing active infection. Symptoms include fatigue, myalgia, arthralgia, paraesthesia, poor sleep, irritability, and concentration difficulties. These have been termed “post-Lyme symptoms” if of short duration or “post-Lyme syndrome” (PLS) if present for more than six months. Symptoms of PLS appear to be similar to those seen in a minority of patients following other systemic infections (so-called “post-infection” or “post-viral” syndromes) and, again, similar to some other infections, are more likely to be present in patients who had severe presentations in the acute illness. 32 Studies of prolonged antimicrobial treatments of patients with PLS have not shown sustained benefit, and have highlighted significant risks of serious adverse events, including central vascular catheter infections, fungal infections, *Clostridium difficile* enterocolitis and biliary stasis.

The concern is that patients with a wide range of conditions including multiple sclerosis, motor neurone disease, autoimmune diseases, arthritis and malignancies have received diagnoses of “chronic Lyme disease” without objective clinical or laboratory support. Many patients have received potentially dangerous treatments, including prolonged courses of antibiotics, antiparasitic and other agents, and have lost opportunities for appropriate management of their conditions.

This can be a very challenging condition for patients and doctors. Please feel free to discuss complex cases with us.

7. I am considering a diagnosis of neurological Lyme disease. What tests should I send?

Send a serum sample for Lyme IgM and IgG, noting the date of likely tick exposure, date of symptom onset and nature of symptoms. Information on country that tick exposure may have occurred in, and any antibiotic treatment already received is useful.

In early Lyme neuroborreliosis, 80% will have positive serology on first testing. If negative, a second serum can be submitted 2-3 weeks later, as paired serum testing will demonstrate a rise in titre or seroconversion, with a sensitivity of 90-100% [4]

Early Lyme neuroborreliosis can manifest as aseptic meningitis, peripheral neuropathy or cranial nerve palsy. Radiculoneuritis usually presents with severe pain. Facial nerve is the most frequently affected cranial nerve and can present as unilateral or bilateral facial palsy. The prognosis of Lyme facial nerve palsy is good, and this phenomenon can be treated as peripheral nervous system Lyme (does not require lumbar puncture and can be treated with PO doxycycline 100mg bd for 14d).

A lumbar puncture should be performed for all cases of suspected Lyme neuroborreliosis (except isolated facial nerve palsy), intrathecal specific antibodies looked for and specific CSF/serum antibody index calculated. Lymphocytic CSF pleiocytosis is characteristic, with raised protein and oligoclonal bands in late Lyme neuroborreliosis. CSF PCR is positive in up to 30% of acute presentations of Lyme neuroborreliosis but rarely useful in late neuroborreliosis.

[4] European Journal of Neurology 2010, 17: 8–16

8. How should I treat Lyme disease?

The oral antibiotics doxycycline, amoxicillin or cefuroxime axetil are recommended for 2 weeks (range 10 to 21 days) for erythema migrans. Facial palsy and other complications need longer treatment (3 to 4 weeks).

The usual adult doses of these antibiotics are:

- doxycycline 100mg twice daily
- amoxicillin 500mg three times daily
- cefuroxime axetil 500mg twice daily.

Doxycycline use is contraindicated for children aged under 12 years and for pregnant and breastfeeding women. Intravenous treatment, usually with ceftriaxone for 2 weeks (range 10 to 28 days), is recommended for some neurological presentations and occasionally for second-line treatment of arthritis and for some other uncommon presentations. The usual adult dose of ceftriaxone is 2g daily.

Erythromycin is not recommended for treating any stage of Lyme borreliosis, as it has a high failure rate.

Longstanding neuroborreliosis may be slow to respond to treatment, as damaged nerve tissue is slow to heal.

Re-treatment may be indicated in occasional cases of neuroborreliosis and arthritis. Seek specialist advice about treatment in difficult cases (see the referral pathway link below).

Useful references

NICE Clinical Guidelines

<https://www.nice.org.uk/guidance/ng95>