Diagnosis and management of patients with Lyme disease:

NICE guideline

INTRODUCTION

The National Institute for Health and Care Excellence (NICE) has published a new guideline on diagnosis and management of Lyme disease.¹ The guideline aims to increase awareness of Lyme disease and ensure that patients get the correct treatment at an early stage.

Lyme disease is a bacterial infection transmitted by the bite of an infected tick. The bacterium *Borrelia burgdorferi* is a spirochete with many similarities to the syphilis organism. Ticks inject a local anaesthetic to the site of the bite and often attach themselves at the hairline or in the axillae or groin areas, so they can be easy to miss.

Ticks are found in grassy and woodland areas, including urban gardens and parks. Not all ticks carry Lyme disease, but infected ticks have been identified in urban and peri-urban areas.² There is a perception that Lyme disease only occurs in certain areas and, although some areas have a higher prevalence, cases are reported throughout the UK. People in certain occupations, for example, farm workers, are at higher risk but anyone who spends time outside is at risk. Worldwide, higher prevalence is noted in Central, Eastern, and Northern Europe, the US and Canada, and parts of Asia. A good occupational, travel, and lifestyle history is important when assessing patients.

Lyme disease is a multisystem illness and can present with a variety of focal and non-focal symptoms and signs. It can cause significant illness and long-term disability. The cause of long-term symptoms is controversial. There is a view that these symptoms are caused by long-term infection, 'chronic Lyme disease', which needs long-term antibiotic treatment. The mainstream medical view is that chronic symptoms can occur after any infectious disease, and damage such as nerve damage from infection may be irreversible and are not an indication of ongoing infection.

There is also interest in the possibility of an immune-mediated process caused by the infection to explain ongoing symptoms but there is not enough evidence for this at present. The guideline does not use the term 'chronic Lyme disease'.

PRESENTATION

Lyme disease may present to general practice in a number of ways:

1. Erythema migrans (EM) — this rash is pathognomonic of Lyme disease and allows a clinical diagnosis of Lyme disease. It is a red rash that increases in size and which may have a central clearing. It can be present from between 3 days to 3 months following a bite and is usually *not* hot, itchy, or painful. The rash usually presents at the site of the bite but may not always. It is possible to get multiple EM. NICE has provided several useful examples on the guideline page of their website (<https://www.nice.org.uk/guidance/ng95/resources/lyme-disease-rash-images-pdf-4792273597>).
2. Non-focal symptoms where more than one of the following is usually present:
 - fevers and sweats;
 - swollen glands;
 - malaise;
 - fatigue;
 - neck pain or stiffness;
 - headache;
 - cognitive impairment; and
 - paraesthesia.
3. Focal symptoms and signs associated with specific organ systems, for example:
 - neurological system, for example, facial palsy, meningitis, mononeuritis multiplex, encephalitis;
 - arthritis — acute inflammation affecting one or more joints that may be fluctuating and migratory;

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- cardiac system — heart block, pericarditis;
- eye symptoms — uveitis or keratitis; and
- skin rashes — acrodermatitis chronica atrophicans or lymphocytoma.

DIAGNOSIS AND MANAGEMENT

A diagnosis of Lyme disease should be made and antibiotic treatment provided for people who have EM.¹ No testing is required.

If focal and/or non-focal symptoms raise the suspicion of Lyme disease, an accurate history should be taken for tick exposure and/or a previous rash that may have been ignored. Many people do not remember a tick bite. Clinical presentation and clinical judgement are an important part of diagnosis and the decision to treat. The bacterium causing Lyme disease is difficult to culture so the current test for Lyme disease is an antibody test. The guideline recommends serological tests for antibody response for presentations other than EM but with a clear steer to treat if the presentation is convincing.

There are issues with testing. Because of the difficulty in culture of *B. burgdorferi* there is no gold standard to evaluate test accuracy. Similar to all antibody tests, if the test is carried out too soon there may not have been time enough for antibodies to be developed. The antibody response will also be affected if people are immunocompromised due to medication or other concurrent illnesses. The guideline recommends repeat testing according to time from development of symptoms. More specialised testing such as use of lumbar puncture, synovial fluid aspirate, or polymerase chain reaction may be required in secondary care settings if there is difficulty in making a diagnosis.

The guideline makes recommendations for antibiotic treatment for different presentations, depending on whether focal symptoms are present, and on the age and weight of the patients. Existing guidelines provide a range of treatment doses and durations but the NICE guideline took a pragmatic approach and aimed for consistency across presentations in terms of drug dosage and treatment duration. The guideline includes a table of antibiotic treatments.¹

No evidence was found to suggest that prolonged courses of antibiotics were beneficial. The guideline does suggest offering a second course of an alternative antibiotic if patients do not improve following the initial course, as the possibility of treatment failure was recognised.

It is useful to note that a Jarisch–

Herxheimer reaction may occur during antibiotic treatment. This can cause fever and an initial worsening of symptoms. It may be confused with an allergic reaction, but it is not and treatment can usually be continued.

REFERRAL

The guideline suggests that children, unless they have an isolated EM, should be discussed with an appropriate specialist. This is both to discuss the diagnosis and to seek advice on antibiotic management. The guideline recommends doxycycline for children between 9 and 12 years, which is in keeping with international practice, but non-specialists may find it helpful to discuss this with a specialist. Specialist referral for adults is recommended if symptoms continue following treatment to either the symptom-specific specialty, for example, rheumatology if the person has joint symptoms, or infectious disease specialists. Referral is to consider further investigation or treatment and to consider other diagnoses.

COMMENT

The published literature on most aspects of epidemiology, diagnosis, and treatment is of low quality. The guideline makes a number of research recommendations covering these areas. It is hoped that GPs will have greater awareness and knowledge of Lyme disease as a result of the guideline and will no longer have mistaken views about where one can and cannot get Lyme disease. The guideline also highlights the range of symptoms that should cause suspicion and the serious manifestations that should not be missed. One of the challenges for GPs is when to suspect Lyme disease among many other more common conditions that have similar symptoms, and how to support people who continue to have symptoms following treatment.

Provenance

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Competing interests

The authors have declared no competing interests.

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