

Q&A with physician-scientist on decoding early Lyme disease

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Every year in the United States, an estimated 476,000 people are [diagnosed and treated](#) for Lyme disease. The estimate comes from the U.S. Centers for Disease Control and Prevention (CDC).

Lyme disease can be treated with antibiotics. The best health outcomes are most likely when a diagnosis is made within the first weeks of infection. If left untreated, the effects of Lyme disease can linger for years and cause [neurological problems](#), arthritis, and a [host of other ailments](#). But because diagnosing Lyme can be difficult, some cases of the disease go undetected long after initial transmission.

To help clinicians improve Lyme disease outcomes, physician-scientists at Rutgers New Jersey Medical School and Stony Brook University have published a guidance article in *NEJM Evidence* on the informed evaluation and treatment of Lyme in its early stages.

Lead author Steven E. Schutzer, a professor of medicine at Rutgers Health, discussed how clinicians can approach patients who have the possibility of an early Lyme disease infection.

Lyme disease is increasingly prevalent and yet many cases go undetected, at least in the early stages. Why is this illness sometimes difficult to diagnose?

The most common sign of Lyme disease is [erythema migrans](#), a bull's-eye or target-like skin lesion that is often the hallmark sign of the Lyme bacterial infection. But that rash doesn't occur in all patients, nor is it always recognized or noticed by patients when it does occur.

Currently, the only Food and Drug Administration (FDA)-approved tests are antibody tests; it can take weeks or longer before a patient mounts a sufficient immune response detectable by these assays.

Another complicating issue is that once somebody has had Lyme disease, they could show positive in the antibody tests for years, to life. This can create a quandary for doctors assessing a patient with a

suspected new case of Lyme disease.

Beyond the rash, what are some other symptoms?

In the early stages, patients might present with a flu-like set of symptoms, but without respiratory symptoms. These symptoms can include fever, headache, muscle aches, joint aches, and fatigue. Patients will likely not have a severe cough, as they would with influenza or another respiratory virus.

Neurological symptoms can also develop, including headaches. But many of these symptoms can be due to other illnesses. For example, meningitis may be due to other microbes and may warrant a spinal tap to get the right diagnosis and treatment.

Because Lyme-infected ticks can also transmit other pathogens, such as those causing [anaplasmosis](#) and [babesiosis](#), patients infected with Lyme have a higher likelihood of co-infections.

What tests are currently available to clinicians for Lyme?

The CDC and others recommend doctors use a two-tier blood antibody (against *Borrelia burgdorferi*-the cause of Lyme) testing approach. The first-tier test, in its most optimal form, is a sensitive semi-quantitative test. It's akin to casting a wide net.

If the test yields a borderline or positive result, it must be followed up with a second-tier test that measures antibodies that are more specific to *Borrelia burgdorferi*. This is used as a confirmatory test.

The most common first-tier type of test is an ELISA. For many years,

the second-tier test was only a Western blot, which provided a visual view of the results. Some of its drawbacks were that interpretation was often subjective and the test itself took more time. A new FDA-approved substitute is to use a second ELISA-type test.

Your paper is designed to assist primary care clinicians in how they should approach a patient with possible early Lyme disease. It's based on recommendations from several leading medical societies and federal public health agencies. Can you provide some specifics?

It's essential that doctors don't get tunnel vision on Lyme. Once antibiotics are administered, they may blunt the patient's antibody response and disrupt what blood tests show.

Thus, doctors should assess the criteria for positivity, and consider mitigating factors. Has the patient been in an endemic area? Are there other skin lesions? Has a neurological exam been conducted to rule out other treatable diseases? Clinicians should always be thinking 'what else can this be, other than Lyme,' and have a low threshold for coordinating with colleagues in other specialties, like neurology and cardiology, to make informed diagnoses and management decisions. This should be an evolving process as new knowledge is acquired.

You also discuss the optimal timing of testing. Can you elaborate?

During the first few weeks of a first-time Lyme infection, the antibody response is usually negative on the conventional two-tier tests before the body has time to mount a detectable immune response. On the other end

of the spectrum, if more than a month has passed since the onset of infection and before treatment, it's more common to have a positive test. It's during this early phase of infection that is the most problematic for doctors.

Most commercial laboratories won't freeze a sample and wait for a second blood draw to test simultaneously. What doctors can do to get around this is to draw a second blood sample and send it to the same laboratory for the same [test](#) and then compare the results to see if there is some evidence of moving toward positivity in the intervening days to weeks before making a diagnosis.

You clearly focused the article on what the clinicians have available now, but what can we expect in the future?

This is not a static field. Researchers are working to develop tests that are even more accurate and can be used earlier. This includes detecting DNA of the Lyme agent.

Researchers are also looking for early molecular messages from the body in response to an infection. Other investigators are working with the help of clinicians on immediate point-of-care tests. Rigorous confirmation of their accuracy and reproducibility would be the intermediary step towards providing them for routine clinical use.

What is the current outlook for most patients?

Fortunately, the outlook is good for most patients with early Lyme disease when an alert clinician recognizes it and begins treatment. Most patients will return to their normal health. The goal of our article is to foster this outcome.

More information: *NEJM Evidence* (2024).

Provided by Rutgers University

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