

MEDICAL RESEARCH

The fight against Lyme disease

James G. Logan hails a study of the controversial tick-borne condition.

It occurs in more than 80 countries and is the most commonly reported vector-borne disease in the Northern Hemisphere. In the United States alone, it spawns 300,000 new cases each year. Yet Lyme disease — caused by species of *Borrelia* bacteria carried by ticks of the *Ixodes* genus — remains one of the most poorly understood infections. It has divided researchers, clinicians and patients, and triggered intense public suspicion and confusion.

So what is science's role in turning the corner on what some have labelled a “public health failure”? Physicians Brian Fallon and Jennifer Sotsky tackle this question in their insightful study *Conquering Lyme Disease*, in which they journey beyond the history, biology and symptoms of the illness. Their greatest accomplishment, by far, is delivering multiple viewpoints with minimal bias and great sensitivity: the clinician's, the researcher's and, particularly, the patient's.

Although recent headlines make Lyme disease seem new, probably the first recorded case was in 1909: the Swedish dermatologist Arvid Afzelius associated a patient's expanding rash (later named *erythema migrans*) with a tick bite. In the 1970s, a link was made to bacteria by rheumatologist Allen Steere; in 1981, the biologist Willy Burgdorfer discovered that the disease was caused by a type of bacterium called a spirochaete. The species complex was named *Borrelia burgdorferi* in his honour. But it was not until the 1990s that US cases were properly reported, through a surveillance system set up by the Centers for Disease Control and Prevention in Atlanta, Georgia.

Since that decade, the global incidence has increased and reporting has improved, as Fallon and Sotsky describe; in the United States alone, known cases have tripled since 1992. There is currently no human vaccine, and research on the

disease has struggled to keep up.

The many presentations of an illness known as the “great imitator”, and its inherent complexities, are why medical communities have often failed to find common ground on diagnosis and treatment, as the authors explore. The manifestations range from no symptoms, or mild influenza-like ones, to severe complications such as inflammation in joints or the brain and persistent neurological problems.

One of the reasons Lyme is difficult to diagnose is that some non-infectious conditions, including fibromyalgia and Alzheimer's disease, present with similar symptoms. The situation is further complicated because *Ixodes* ticks transmit a host of other pathogens, such as *Rickettsia*, other bacteria, viruses and protozoa, leading to diseases including typhus, relapsing fever, babesiosis and meningoenzephalitis. Misdiagnosis is thus all too common.

Treatment is also far from straightforward.

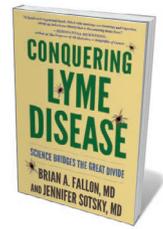
Although antibiotics can clear infection in some cases, Fallon and Sotsky describe how genetic differences in *Borrelia* bacteria found on different continents make treatment difficult. There are, for instance, three different species in the complex in Europe. The authors note that each can cause different symptoms in people with Lyme disease who develop neurological complications. So a treatment that works for one species of the bacterium may not work for another.

And spirochaetes can remain in the body even after courses of antibiotics (E. Hodzic *et al. Antimicrob. Agents Chemother.* **52**, 1728–1736; 2008). Fallon and Sotsky hypothesize that they may “hide” inside human cells, for instance. A big question is whether the spirochaetes that hang on in this way can replicate and cause disease.

Whatever the mechanism, proof of the existence of persistent symptoms will pave the way for better diagnostics, treatment and care. Some patients have spent years trying to convince medical doctors that their symptoms remain after treatment. Fallon and Sotsky strikingly convey these people's difficulties and frustrations. Clinicians, for instance, might fail to ask the right questions. People with chronic Lyme disease can feel abandoned, and even suicidal. That has led to protests and court hearings, notably in the United States. But these people, the authors argue, have played a significant part in moving understanding beyond conventional thinking, and ultimately driving research forward. Clinicians are now beginning to acknowledge both the complexity of Lyme disease and patients' needs.

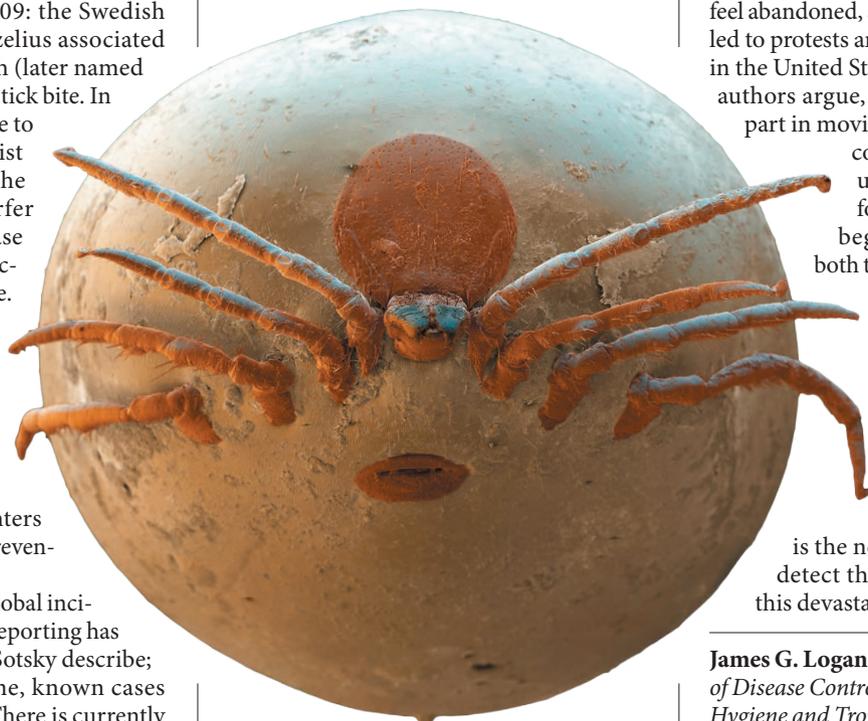
Fallon and Sotsky end on a firmly positive note, reviewing avenues for new research across many disciplines, from diagnostics to vaccines and treatments. What's particularly pressing is the need for a definitive test to detect the spirochaetes that cause this devastating disease. ■

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Conquering Lyme Disease: Science Bridges the Great Divide

BRIAN A. FALLON & JENNIFER SOTSKY
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Ixodes ticks spread Lyme disease.

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