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Arno Karlen: The biography of a germ

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Lyme disease, an unpredictable inflammatory disorder, has become the most common arthropod-borne infection in the United States. It occurs in the coastal regions of the northeast, but also in the midwest and western states. The white-footed deer mouse (*Peromyscus*) transmits the disease to humans by the bite of an immature tick, *Ixodes dammini*. Lyme disease is correlated with the presence at the bite site of the spirochete *Borrelia burgdorferi*, named after Willy Burgdorfer, who isolated the bacterium in 1982 at the Rocky Mountain National Laboratory, Colorado. A tick-borne associated syndrome had already been observed in Europe in 1908 by Arvid Afzelius. The European tick associated with the disease is *Ixodes ricinus*. The disease was first recognized in 1975 in the United States, and in 1977 Allen C. Steere and his team at Yale University began to unravel the details. They reported an epidemic of arthritis in residents of several Connecticut communities that began in 1972 and saw the tick connection. Although early symptoms are mild, if untreated, the illness can be painful and serious.

In the middle of the 1970s, two Connecticut children were diagnosed with juvenile rheumatoid arthritis. Their symptoms were swollen joints, fever, sore throats, headaches, fatigue and depression. Not being satisfied with the medical explanation, Polly Murray, the mother of one of them, took her evidence for an epidemic of similar symptoms in Lyme, Connecticut, to Steer. When he plotted the frequency of acute arthritis and similar complaints in Lyme, East Lyme and Haddam, he realized that the illness was not limited to children (Polly Murray herself had been sick during the 15 years she lived in Lyme). It correlated with grassy woodlands, and most of the afflicted fell ill in summer or early autumn. Not a single patient, and there were more than 50 in Steere's first cohort, resided in the heavily populated urban areas of Connecticut. At least one in four patients recalled that they

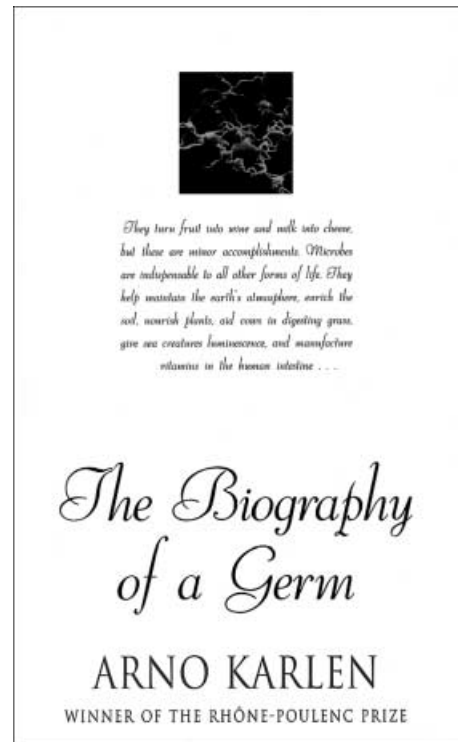


Fig. 1 Arno Karlen, The biography of a germ

had been bitten by ticks. The symptoms of the mysterious Lyme disease of Connecticut had broadened by the time Steere published his 1979 paper (Steere and Malawista (1979) *Ann Intern Med* 91:730). Since then, Lyme disease is no longer a medical curiosity. A commonality was recognized with several northern European illnesses: acrodermatitis chronica, erythema migrans and erythema chronicum migrans, among others. The disease shows three clinical stages; the distinctive rash (called erythema chronicum migrans), heart and nervous disorders. These have been found in thousands of victims, many of whom live beyond the borders of Connecticut.

The *Biography of a Germ* (Fig. 1) describes the source of the problem (essentially a symbiosis between different types of organisms) and its history. In the 1920s, the Murray house was surrounded by sparse vegetation and a few lone trees. By the 1970s, “the land about our house was thick with trees, wild roses, barberry, bittersweet, wild grapevines and other vegetation.” In summer, the family and their neighbors might pick a dozen ticks a day off their children and pets, including “seed ticks,” tiny nymphal stages of the deer tick.

Willy Burgdorfer, a Swiss-born medical researcher who had studied tick-borne disease since the 1950s, was the first to make the connection between habitat and symptoms. Burgdorfer knew that deforestation, by transforming the countryside into grazing and mining country, had converted the landscape into a perfect habitat for mice and ticks. When ticks became rare and their habitats and those of the small mammals they bite were replaced by Rocky Mountain shopping malls and asphalt parking lots, the “spotted” fever disappeared. When woods, shrubs, grass and other suburban greenery reappeared, the Rocky Mountain spotted fever re-emerged too. Burgdorfer was aware of the pioneering work of Howard Ricketts on tiny intracellular bacteria that were later called *Rickettsia*. He also knew that two Swedes, Carl Lennhoff, in 1948, and Sven Hellstrom, in 1949, had suggested that erythema chronicum migrans with meningitis probably was caused by a tick-borne spirochete bacterium sensitive to antibiotics.

From 1981 on, Burgdorfer dissected more than a hundred ticks collected at Shelter Island, off the Long Island coast of New York; he found that two thirds of them bore spirochetes. Shelter Island provided wonderful scrubby grassy woodland habitat for both deer mice and deer. Burgdorfer obtained blood samples from Shelter Island patients. Antibodies indicated that these people had been exposed to the same spirochete bacteria as those carried by the ticks. After his findings were published in 1982, the elusive spirochete (a bacterium that appears as “the silhouette of a corkscrew” unless it is stained with heavy metals and studied by high mag-

nification electron microscopy) was named *Borrelia burgdorferi*. Certainly Burgdorfer deserved this recognition. The insect-borne genus was named for bacteriologist Amédée Borrel (1870–1961).

Alan Barbour’s development of appropriate media permitted the growth in culture of *B. burgdorferi*. After cultivation, Burgdorfer could establish the definite cause of Lyme disease. *B. burgdorferi* is related to other *Borrelia* bacteria, whose presence has been correlated with symptoms of relapsing fever carried by soft ticks or lice. Recent experimental work by the Norwegian brothers Oystein and Sverre-Henning Brorson have verified the viability of “round bodies” in vitro – these may explain why disease symptoms reappear in people who no longer seem to harbor spirochetes.

The *Biography of a Germ* is not a scientific book at all. Karlen’s account is instead a delightful and witty page-turner. He commits the typical sins of many popularizers: glibness, sloppiness and factual errors. However, interested readers forgive the ardent author’s facile style, in the same way that one does not expect a physician telling a complicated story at a cocktail party to be accurate. From the dust-jacket hype that claims a sex life for the spirochete, which has none, and a tree of life for Linnaeus (Linnaeus believed in the fixity of the species and never subscribed to any evolutionary tree of life), to the folk classification employed by the author, exaggerations abound. Karlen’s living world is divided into four kinds of life: plants, animals, germs and people. The reader is warned to remain skeptical. The details of Karlen’s story are not to be taken literally. Read it for what it is: an informative, charming, serendipitous and sometimes opinionated talk that successfully transmits the historical and environmental activities of the *Borrelia* spirochete in generating disease symptoms. It helps us to understand the way in which infectious diseases are population-density- and habitat-dependent. The ecology of the white-tailed deer, the deer mouse, the deer tick and the suburban home owner are relevant. The story line reveals the extent to which Lyme disease in all its guises is essentially a finely honed serial symbiosis.