A Tale of Two Spirochetes: Lyme Disease and Syphilis

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Two spirochetal infections hold fascinating positions in the history of infectious diseases. Numerous historic and literary figures were believed to have neurosyphilis, which consequently has been blamed for otherwise inexplicable developments in Western European history. More recently, Lyme disease has served as a focal point for the divide between evidence-based medicine and traditional experiential approaches, highlighting issues of physician autonomy in an era of guideline development, and epitomizing the tension between patient advocacy and scientific medical care.

How is it that spirochetal infections can play such outsized roles? Several biologic and sociologic factors are probably relevant. Both can affect the nervous system, and for patients and most physicians, few things are more unnerving than disorders that may affect brain function. Both can be chronic. Although both *Treponema pallidum* and *Borrelia burgdorferi* are highly sensitive to antibiotics, without appropriate treatment, these slowly multiplying, not very immunogenic organisms can persist in relatively immune-protected sites for years, gradually resulting in end organ damage.

Most significant is the societal context in which these diseases first appeared. Syphilis invaded Europe when biologic understanding of disease was limited. In the absence of knowledge of other diseases, and with few tools to diagnose syphilis unequivocally, all manner of clinical phenomena were blamed on this infection. Lyme disease was described at a time of far greater scientific understanding. However, the inaccurate notion that this is a novel infection for which diagnostic tools are limited, and the availability of the Internet to enable widespread but uncritical proliferation of information have contributed to an unfortunate degree of misunderstanding. At a time when the population is inadequately scientifically literate but simultaneously suspicious of organized medicine and sympathetic to populist outpourings,

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this has allowed the widespread acceptance of scientifically invalid information, culminating in state legislatures passing laws requiring insurance companies to pay for treatment that has been shown to be irrelevant, unhelpful, and, in fact, harmful.

LYME DISEASE

The terms *Lyme arthritis* and *Lyme disease* were coined in the mid-1970s when a large number of children near Lyme Connecticut were diagnosed with what seemed to be juvenile rheumatoid arthritis.[1] In response to vigorous advocacy by the children's parents, a series of epidemiologic studies rapidly identified the cause as a novel tick-borne spirochete, *B burgdorferi*. As more was learned about this infection, experts realized that it was remarkably similar to a group of disorders identified early in the twentieth century in Europe, and ultimately that all of these disorders were caused by infection with closely related organisms.

In Europe, four strains, all belonging to the *B burgdorferi sensu lato* group, have been identified: *B burgdorferi senso stricto, B garinii, B afzelii*, and *B spielmanii*.[2] In the United States, only the first has been found.[3–5] The general belief is that the disease was introduced into the United States when a herd of infected deer was imported from Europe early in the twentieth century. All four strains consist of motile corkscrew-shaped bacteria, typically approximately 0.2 to 0.3 μm in diameter, and 20 to 30 μm in length. Their entire genome has now been sequenced.

The clinical disorders described in Europe and those in the United States have some differences. Arthritis seems to be more common in patients in the United States, whereas painful radiculitis and encephalomyelitis are more frequent in Europe. However, rheumatism was described in one of the earliest European descriptions of this disorder.[6] Although these differences have several possible explanations, they are probably caused by a combination of bacterial strain differences and ascertainment bias. The systemic disease is largely treated by neurologists in Europe and by rheumatologists in the United States.

Regardless of the strain, transmission occurs virtually exclusively by bites of hard-shelled *Ixodes* ticks; *I scapularis* in North America, and *I persulcatus, I ricinus*, and others elsewhere in the world. The host–vector relationship depends on several unique features, including the feeding cycle of these ticks. Larval ticks hatch uninfected from eggs and then have their first blood meal, typically on small mammals such as field mice. If that host is infected, the tick can become infected, with spirochetes then residing in their gut. Months later, when as a nymph they have their second blood meal, they will have either a second opportunity to become infected or their first opportunity to infect a new host, which is more often a larger mammal, including potentially humans.

When ticks attach to feed, they inject saliva into the host, saliva that contains local anesthetics, anticoagulants, and other bioactive molecules to allow uninterrupted feeding for up to several days. When blood arrives in their gut, this triggers spirochete proliferation. Spirochetes then disseminate throughout the tick, particularly invading the tick salivary glands, a sequence of events that requires at least 24 hours. At that point, injection of additional saliva can result in injection of viable spirochetes. Consequently, infected ticks must remain attached for at least 24 hours before hosts are at significant risk for infection.[7]

After inoculation into the new host, spirochetes proliferate locally. Within days to, at most, weeks, this results in a local erythema, erythema migrans (EM), that has virtually unique characteristics. As spirochetes migrate outward, the area of erythema gradually expands, growing to many centimeters in diameter. Characteristically, EM grows