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Lyme disease: scratching the surface

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The excellent Comment by Ulrike Munderloh and Timothy Kurtti (Sept 17, p 962)1 describes the complex life cycle of Borrelia burgdorferi, the spirochaetal agent of Lyme disease, as it traffics between tick and mammalian hosts. The Comment highlights a growing problem with Lyme disease: while what is known about the basic science of this tick-borne illness becomes more complex, the clinical science remains relatively simplistic and uninformed.2 This divergence has produced a disconnection between the recognition of B burgdorferi as one of the most invasive and elusive bacteria known to man, and the clinical perception that Lyme disease is "hard to catch and easy to cure".

The complexity of the Lyme disease spirochaete goes beyond the features described by Munderloh and Kurtti. With more than 1500 gene sequences, B burgdorferi contains at least 132 functioning genes; by comparison, the spirochaetal agent of syphilis, Treponema pallidum, contains only 22 such genes.2 Furthermore, the Lyme disease spirochaete contains 21 plasmids (nine circular and 12 linear).2 This is by far the largest number of plasmids found in any known bacterium, and the large number of plasmid genes is thought to provide a rapid response system that allows the spirochaete to cycle efficiently between ticks and mammals.3 Gene exchange and plasmid transfers among Borrelia strains can also increase the pathogenicity of the organism.3

In the mammalian milieu, B burgdorferi uses the host fibrinolytic system to penetrate the blood-brain barrier and gain access to the central nervous system. The Lyme disease spirochaete contains a secretory mechanism for porin, adhesin, and haemolysin proteins, and these secreted products can contribute to the invasive properties of the organism.4 The spirochaete can enter cells such as fibroblasts, synovial cells, endothelial cells, and macrophages. In these cells, it becomes functionally resistant to treatment, partly due to "camouflage" proteins produced by itself or adsorbed from the cell, and partly due to altered morphology as the spirochaete assumes a non-replicating cyst form.2 The immune evasion strategy used by B burgdorferi is similar to strategies used by the mycobacterial agents that cause chronic infections such as tuberculosis or leprosy.2 These organisms also exist as non-replicating cyst forms that can be "resuscitated" by autocrine cytokine-like factors after lying dormant for months. B burgdorferi has been shown to use luxS, an autoinducer gene used by other bacteria, to regulate replication.5 It is the first time that this autoinducer gene has been identified in a spirochaete. Thus the combination of genetic complexity, intracellular localisation, immune evasion, and autoregulation makes the Lyme disease spirochaete a formidable infectious agent.2

By contrast with the complex basic science of B burgdorferi outlined above, a popular clinical notion is that Lyme disease can be cured with 2–4 weeks of antibiotics. Although this might be true of promptly treated acute B burgdorferi infection, chronic infection that allows the spirochaete's complex pathophysiological mechanisms to unfold can result in tenacious tissue invasion that is extremely difficult to eradicate. Understanding the pathophysiological complexity of this organism should help to

improve our clinical approach to Lyme disease.2

We declare that we have no conflict of interest.

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