Persister cells still a problem for Lyme disease patients

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There is increasing evidence of bacterial persistence in microbiology. “Though its applicability to *B. burgdorferi* has been controversial, persistence is a widely-accepted phenomenon in microbiology which in some instances can have therapeutic implications,” according to Cabello. [1]

“While still a matter of dispute, there are numerous reports of antimicrobial treatment unable to completely eliminate *B. burgdorferi* from the tissues of experimentally infected rodents and nonhuman primates.”

The ability of spirochetes to survive in a tick followed by an animal and back to the tick may explain the persister cell. The metabolic and morphologic changes needed by the spirochete to survive both the tick and vertebrate reservoir may explain “tolerance to otherwise lethal doses of antimicrobials and to other antimicrobial activities,” he points out.

Borrelia burgdorferi, the spirochete that causes Lyme disease. (Source: CDC)

Spirochetes can become tolerant to antimicrobials through phenotypic changes. Phenotypic changes typically involve adaptation to the environment without a genetic change. For example, spirochetes are covered with Outer surface protein A (OspA) in the tick and covered with Outer surface protein C (OspC) in vertebras.

Spirochetes can also adapt in culture. “Stationary phase *B. burgdorferi* cells in culture can also become phenotypically tolerant to antimicrobials used in treating Lyme borreliosis such as ceftriaxone, doxycycline, and amoxicillin,” according to Cabello.

His examples included, “Readily detectable *borrelia* tolerant to antimicrobials in suspension cultures and biofilms in vitro, potential refugia for persister spirochetes and apparently quiescent round forms under several kinds of environmental stresses.”

Refugia refers to potentially protected areas for spirochetes. “*Borrelia burgdorferi*, the tick-transmitted etiologic agent of Lyme borreliosis, can colonize and persist in multiple tissue sites despite vigorous host immune responses,” writes Cabello in his 2007 paper in *Trends in Microbiology*. [2]

“In infected vertebrate hosts, such refugia could be found in collagenous and other avascular tissues where borrelia are not multiplying.”

The presence of persisters may facilitate emergence of antimicrobial-resistant bacteria. “It should be noted that although persistence is phenotypic, the presence of persisters can also facilitate emergence of

genetically antimicrobial-resistant bacteria, e.g., by mutation," according to Cabello.

References:

1. Cabello FC, Godfrey HP, Bugrysheva J, Newman SA. Sleeper cells: The stringent response and persistence in the Borreliella (Borrelia) burgdorferi enzootic cycle. Environ Microbiol. 2017.
2. Cabello FC, Godfrey HP, Newman SA. Hidden in plain sight: Borrelia burgdorferi and the extracellular matrix. Trends Microbiol. 2007;15(8):350-354.
