An antibiotic for Lyme disease

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Fascinating research reports that hygromycin A, an antibiotic identified in the 1950s and long since discontinued, has surprisingly high activity against the bacteria responsible for Lyme disease.

One concrete consequence of climate change is the increased risk of transmission of infectious diseases by vectors such as mosquitoes and ticks. Global warming is promoting the geographic expansion of several of these vectors, which is causing more and more people to be exposed to certain pathogens.

The outbreak of Lyme disease in southern Canada, including southern Quebec, is a good example of this phenomenon. This disease, which originated in New England (it was first described in the town of Lyme, Connecticut, hence its name) is caused by the spirochete bacteria *Borrelia burgdorferi* and transmitted by the bite of a tick called *Ixodes scapularis*. The disease began to manifest itself in southeastern Canada in the early 2000s, and data indicates that rising temperatures have caused the *I. scapularis* tick's territory to expand northward, at a rate of about 33 at 55 km per year (1). It is for this reason that the annual incidence of Lyme disease has skyrocketed in recent years in Canada, from 40 cases in 2004 to almost 1,000 cases in 2016.

POOR PERFORMING ANTIBIOTICS

Infection with the bacteria *B. burgdorferi* very often causes a rash called erythema migrating at the site of the tick inoculation. From there, the bacteria can spread rapidly not only through the skin, but also through the heart and nervous system and cause myocarditis, painful (radiculitis) or paralyzing nerve inflammation, and meningitis.

Clinically, the disease is treated with broad-spectrum antibiotics such as doxycycline, amoxicillin, and ceftriaxone. These non-specific treatments, however, cause considerable side effects for patients, as they destroy the gut microbiota, the bacterial community that plays countless crucial roles in the maintenance of good health, and furthermore, promote the proliferation of opportunistic resistant bacteria (enterococci, for example) which take advantage of this to establish themselves and disrupt the gastrointestinal balance. The identification of more specific antibiotics is therefore clearly desirable to improve the treatment of this disease.

REDISCOVERY OF AN ANTIBIOTIC

To identify this type of antibiotics, a team of American microbiologists used as starting material hundreds of extracts from actinomycetes, a group of filamentous bacteria widespread in the environment and which are known to produce several bactericidal compounds (2). To their surprise, the only compound with strong antibiotic action specific to *B. burgdorferi* that could be identified by this approach was hygromycin A, an antibiotic isolated almost 70 years ago and which had never been really used clinically because of its low activity against most bacteria.

This specific action of hygromycin A against *B. burgorferi*, combined with the lack of effects against most other groups of bacteria, is of great interest, as it could potentially treat Lyme disease without causing the typical side effects, especially intestinal, from broad-spectrum antibiotics.

Preliminary studies carried out on animal models support this point: oral administration of the antibiotic to mice infected with *B. burgdorferi* made it possible to cure the infection, without significant effect on the composition of the intestinal microbiota of the animals. Since wild mice represent one of the main natural reservoirs of this bacterium, these results allow us to consider the use of bait for wild mice, which would contain hygromycin A to eradicate this pathogen at the source, before it can be transmitted to humans through ticks.

Much work remains to be done, but these results make it possible to envision for the first time the development of a specific antibiotic treatment for Lyme disease and to avoid the disastrous complications often associated with this disease and with current treatments.

(1) Leighton PA et al. Predicting the speed of tick invasion: an empirical model of range expansion for the Lyme disease vector Ixodes scapularis in Canada. J. Appl. Ecol. 2012; 49 : 457-464.

(2) Leimer N et al. A selective antibiotic for Lyme disease. Cell 2021 ; 184 : 5405-5418.e16.

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