New Dapsone Study: Breaking Biofilm

New in vitro study on dapsone (diaminodiphenyl sulfone), and dapsone combination therapy (DDS CT) was just published by Dr. Richard Horowitz et al. and provides hope of effective treatment for patients with persistent Lyme disease.

The study is suggestive that dapsone combination therapy may well characterize both a novel and successful option to treat Borrelia burgdorferi persister cells in the form of biofilm. There are several hypotheses causing great controversy regarding the persistent symptoms that greater than 10-20% of patients are experiencing after infection with B. burgdorferi. The study evaluated the effectiveness of dapsone against B. burgdorferi biofilm forms of the bacteria by testing in individual as well as in combination therapy with several
drugs including cefuroxime, doxycycline, rifampin, and azithromycin *in vitro*.

The results were robust, showing that using dapsone alone or in various combinations with the above stated drugs significantly reduced the mass and protective glycosaminoglycan layer affecting the capability of the biofilm form of *B. burgdorferi*. DDS CT efficacy on the *B. burgdorferi* biofilms was also determined by ascertaining the biofilm polysaccharide matrix content, glycosaminoglycans (GAG).

Study results showed the most efficient single use antibiotic at reducing biofilm was dapsone at both 10 µM and 50 µM concentrations, showing 69% and 58% residual viability respectively. Used individually, other antibiotic treatments (doxycycline, cefuroxime, and azithromycin) proved to be less efficient and, in some cases, even caused an increase biofilm mass. In contrast, triple and quadruple combination antibiotic therapies showed greater efficacy. The most significant finding was that dapsone used individually or in combination therapy with rifampin, and a tetracycline and/or a macrolide and/or a cephalosporin showed great promise in the treatment of persistent Lyme patients, with prior clinical studies demonstrating improvement in many of the debilitating symptoms that patients suffer including fatigue, pain, neuropathy, sleep disturbances, cognitive dysfunction, sweats and flushing. It is urgent that randomized trials are launched to evaluate the clinical effectiveness of DDS CT as the spread of Lyme disease continues to increase on a global scale.

**Read the full journal article:** Effect of dapsone alone and in combination with intracellular antibiotics against the biofilm form of *B. burgdorferi*

**Read the 2016 article:** The Use of Dapsone as a Novel “Persister” Drug in the Treatment of Chronic Lyme Disease/Post Treatment Lyme Disease Syndrome
Bat Tick: Researchers Identify Carios kelleyi in New Jersey

Live larval bat tick (Carios kelleyi) removed in 2019 from big brown bats in Mercer County, New Jersey. Photo: J. Occi/Rutgers Center for Vector Biology

In a recent Rutgers University-led study, researchers identified *Carios kelleyi*, a “soft” tick species associated with bats, for the first time in New Jersey. This parasite, of almost exclusively bats, is thought widespread in the US (as well as parts of Canada, Mexico, Costa Rica, and Cuba), with known occurrences in 29 of the 48 contiguous United States. Larvae collected from big brown bats (*Eptesicus fuscus*) in Mercer and Sussex counties were confirmed as *C. kelleyi* and added to the list of New Jersey ticks.
The risk of this tick to human health in New Jersey is unknown although *C. kelleyi* has been reported to feed on humans in other states. Unlike hard ticks, soft ticks feed multiple times over many years for short periods of time, with blood meals lasting just minutes to hours. The species of bats that host these ticks commonly roost in human-made structures such as attics of homes as well as barns. When not host-seeking or feeding, these ticks shelter in the cracks and crevices of bat roosting structures and may not be easily surveyed or detected. Occupants of these structures including humans, pets, and livestock, may potentially be bitten without awareness of these parasites. In other states, microbes, including a novel spotted fever *Rickettsia*, a novel relapsing fever-related *Borrelia*, and *Bartonella henselae* have been found in *C. kelleyi*. These microbes can be harmful to humans, pets, and livestock, and more research is needed to assess the medical and veterinary significance of these ticks.

The Lyme Disease Association (LDA) thanks study lead author, James L. Occi, who is also a member of the LDA’s Scientific & Professional Advisory Board, for his continued research on ticks and tick-borne diseases and for the tick photos he
Study Reveals Some Tick-Borne Pathogens Found in Fleas

In a recent study conducted in central Pennsylvania, evidence of emerging pathogens, some also common to ticks, have been found in fleas. Various pathogens can be spread by ectoparasites among animal host populations in nature. Along with ticks, fleas are found to commonly infest small mammals. The role of pathogen transmission cycles for these vectors is
In this study, small mammals were captured and fleas were collected in an effort to better understand the enzootic cycle of flea-borne pathogens in central Pennsylvania. Pathogen testing was conducted in both the small mammal hosts and the fleas collected.

Seven species of small mammals were captured of which white-footed mice (*Peromyscus leucopus*) and southern red-backed voles (*Myodes gapperi*) accounted for over 94% of the captures. Only *P. leucopus* tested positive for the blood-borne pathogens examined, with 47 (18.1%) positive for *Anaplasma phagocytophilum* and ten (4.8%) positive for *Babesia microti*.

Of the 61 fleas collected from small mammals and tested for pathogens, *Orchopeas leucopus* was the most common flea species. Pathogenic bacteria and parasites were detected in 33.3% of total fleas collected, and included *Bartonella vinsonii* subspecies *arupensis*, *B. microti*, and a *Rickettsia felis*-like bacterium. Researchers believe this to be the first report of *B. microti* DNA detected from a flea, as well as the first report of a *R. felis*-like bacterium from rodent fleas in eastern North America.

At this time, only plague (*Yersinia pestis*) is a nationally reportable flea-borne disease in the United States. Like tick-borne diseases, under-reporting of flea-borne illnesses limits understanding of the burden of disease from these vectors. The potential for new and re-emerging pathogens in fleas as well as the potential for fleas to play a role in natural transmission cycles of tick-borne pathogens is not understood. This study elucidates that further investigation is needed to understand the ecology of flea-borne disease transmission cycles, vector competence of fleas for tick-borne pathogens, and the risk to human health.

Read full article: Host distribution and pathogen infection of
fleas (Siphonaptera) recovered from small mammals in Pennsylvania

Asian Longhorned Tick Continues to Multiply, Can transmit to Animals in the Lab

These pictures of the *Haemaphysalis longicornis* (Asian longhorned) were taken recently by LDA’s Scientific & Professional Advisory Board member James L. Occi, Rutgers, in Bergen County NJ. The invasive tick was first discovered on a NJ farm on a sheep in 2017. The tick probably came from Asia, where it is able to transmit diseases to cattle, other
animals, and to humans and is now found in 12 states. One of the greatest concerns is about its parthenogenetic ability, the female reproduces without the male. This enables the tick to quickly become an established species in an area. It has already killed cattle in a couple states where more than a thousand ticks were found on each of the deceased animals.

To date, the Asian longhorned tick has been found in the laboratory to be able to acquire and transmit *Rickettsia rickettsii*, the agent of Rocky Mountain spotted fever (RMSF) and was also found to be able to transmit *R. rickettsii* through the ova (Stanley et al, 2020).* The Asian longhorned tick has not been found to transmit to humans outside the lab at this time in North America.

However, we need to be cautious, since until several years ago, the government indicated that brown dog ticks only fed upon dogs, not people. Therefore humans did not have to worry about getting RMSF from a brown dog tick. Now we know that human transmission is happening from the brown dog tick, since we know they are biting humans, especially in the Southwest.

*https://academic.oup.com/jme/article/doi/10.1093/jme/tjaa076/5822589


Current Lyme Disease Testing Problems

Elizabeth Maloney, MD, explains current Lyme disease testing issues, including the ELISA and Western Blot, sensitivity and specificity of the testing, and the problems associated with the two-tier testing recommended by the CDC. It begins with the general characteristics of diagnostic testing.

The Summary states: “Serologic testing for Lyme is inaccurate. While the inadequate sensitivity of ELISA and Western blot tests is the primary problem, imprecision and the lack of clinical validity contribute to the poor performance of two-tier testing in clinical settings. Although the high specificity of the CDC two-tier strategy works well for epidemiologic purposes, the testing sequence reduces the overall sensitivity, thereby limiting its clinical effectiveness. While positive results on two-tier testing in an untreated patient who has symptoms of Lyme disease would confirm the clinical diagnosis (and it would be a mistake to label such results as “false positives”), negative results do not rule out Lyme disease.”

See full article by Elizabeth Maloney, MD here: Applying Basic Concepts in Laboratory Testing to Serologic Testing for Lyme Disease

See International Lyme & Associated Diseases (ILADS) Controversy & Challenges Page – Issues with Diagnosis & Diagnostics
NIH Releases Strategic Plan for Tick-Borne Disease Research

The NIH Strategic Plan for Tickborne Disease Research, October 9, 2019, is good news for everyone in the Lyme and tick-borne diseases community! The plan builds on the activities of the Department of Health and Human Services Tick-Borne Disease Working Group (TBDWG), which issued a 2018 report to Congress.
outlining research recommendations. Through inventories sent
to government agencies to determine gaps in their research on
tick-borne diseases (TBD), the Working Group uncovered the
fact that NIH did not have a national strategy for TBD. The
HHS TBDWG Report made the recommendation below in the November
2018 report:

**Recommendation 8.1:** NIH: Create an NIH tick-borne disease
strategic plan, with public input during creation and
implementation, to address tick-borne diseases, including all
stages of Lyme disease. Include in the strategic plan the
coordination of research funding across NIAID, NINDS, NIAMS,
and NIMH to increase knowledge of pathogenesis, improve
diagnosis, and develop and test new therapeutics for tick-
borne diseases. Update every five years.

The LDA President, Pat Smith, served as a TBDWG member that
wrote the 2018 report. She was reappointed this year for a
second term as it develops the next report to Congress due
December of 2020.

In developing this strategic plan, as recommended by the TBDWG
Report, NIH sought input from the research and medical
communities, patient advocacy groups, pharmaceutical industry,
and the general public.

The Lyme Disease Association submitted input to the NIH on a
strategy:

https://lymediseaseassociation.org/news/lda-provides-input-to-
national-institutes-of-health-strategic-plan-development

The newly released NIH plan focuses on five scientific
priorities important for advancing research and development
over the next five years.

1. Improving fundamental knowledge of tickborne diseases,
   including the biology of tickborne pathogens; how they
   are transmitted to humans, evade the immune system, and
spread within the body. Including determining the cause of persistent symptoms in some people infected with tickborne diseases, such as Lyme disease, and furthering the understanding of how tick-derived factors contribute to the establishment and severity of disease.

2. Advance research to improve detection and diagnosis of TBDs. Improving detection and diagnosis of tickborne diseases by developing rapid diagnostic tests that can detect a pathogen both early and late in infection and distinguish between active and past infections. NIH will support the development of diagnostics capable of predicting treatment success and identifying human biomarkers of infection and persistent symptoms.

3. Accelerate research to improve prevention of TBDs. The new plan also prioritizes the acceleration of research designed to prevent tickborne disease infection, including vaccines, and immune-based treatments, as well as strategies to reduce the transmission of tickborne pathogens to animal populations that serve as hosts.

4. Focusing on research to develop new treatments for tickborne diseases and techniques to reduce disease complications.

5. Prioritizing the development of tools and resources to advance tickborne disease research by improving scientists’ access to biological samples, tickborne disease genetic data, and supporting preclinical development of promising products.

NIH intends to expand collaborations across its institutes and centers to promote a multidisciplinary approach to tickborne disease research, answer complex biological questions and encourage the application of state-of-the-art technologies used successfully in a range of scientific disciplines.

NIH Strategic Plan for Tickborne Disease Research

NIH Strategic Plan News Release
Congressman Smith praises NIH announcement (TAPinto.net)

Congressman Smith press release on NIH Strategy

Note from LDA: tick-borne disease is generally spelled with a hyphen. NIH has chosen to leave out the hyphen in its report.

LDA Celebrates 50!

In 2018, Lyme Disease Association Inc. (LDA) reached a milestone in its Lyme research support—the 50th journal article with LDA supported research was published. Articles found in 39 different journals begin in 1996 with the ground-breaking, Borrelia burgdorferi DNA in the Urine of Treated Patients with Chronic Lyme Disease Symptoms: A PCR Study of 97 Cases, by the late Manfred Bayer in the journal Infection.

Journals range from The Proceedings of the National Academy of Science, Neurology, Genetics, Gene, Emerging Infectious Diseases, Journal of the American Medical Association, Biochemistry, Veterinary Sciences, Clinical Infectious Disease, Journal of International Neuropsychological Society to the most recent, Ticks and Tick-Borne Diseases.

Researchers funded include, Drs. Ying Zhang, Brian Fallon, Ed Breitschwerdt, Steven Schutzer, Travis Taylor, Eva Sapi, Kerry Clark, Ben Luft and many more from across the U.S.

Other ground-breaking studies include:

- The Underdiagnosis of Neuropsychiatric Lyme Disease in
Children and Adults.
- A randomized, placebo-controlled trial of repeated IV antibiotic therapy for Lyme encephalopathy.
- Whole-Genome Sequences of Thirteen Isolates of Borrelia burgdorferi.
- Absence of Borrelia Burgdorferi-specific immune complexes in chronic fatigue syndrome.
- A Drug Combination Screen Identifies Drugs Active against Amoxicillin-Induced Round Bodies of in Vitro Borrelia burgdorferi Persisters from an FDA Drug Library,
- Characterization of Biofilm Formation by Borrelia burgdorferi In Vitro.
- Borrelia Burgdorferi–Specific Immune Complexes in Acute Lyme Disease.
- A Controlled Study of Cognitive Deficits in Children with Chronic Lyme Disease.
- Severity of Lyme disease with persistent symptoms: Insights from a double-blind placebo-controlled clinical trial.
- Distinct Cerebrospinal Fluid Proteomes Differentiate Post-Treatment Lyme Disease from Chronic Fatigue Syndrome.
- Regional prevalences of Borrelia burgdorferi, Borrelia bissettiae, and Bartonella henselae in Ixodes affinis, Ixodes pacificus and Ixodes scapularis in the USA.

Click here to link to all 50!

Other

They are many articles published by people outside the field such as reporters and patients that may be of interest to those researching Lyme disease. Experiences with OCD
There are articles that are published on Lyme disease which are not published in journals which are subject to peer review process but which, nonetheless, are valuable tools for anyone interested in the disease. They may be written by doctors, scientists, government officials, advocates, others considered experts in the field.

The Effects of Lyme Disease on Students, Schools & School Policy

You Can Make a Difference to a Child by Reducing Risk of Lyme Disease
by: Network to Reduce Lyme Disease in School-Aged Children (includes the EPA, CDC, LDA)

*NASN School Nurse.* 2010; 25: 110-113

nas.sagepub.com/cgi/reprint/25/3/110  (leaving the LDA website)

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These articles carry the most scientific weight as they are reviewed by a committee of doctors and scientists before they are accepted for publication.

The following links are provided for you to other sites which
have lists of scientific publications on Lyme disease where you can search for particular aspects of the disease. Sorry, but LDA does not have staff to help you search. You are leaving the LDA website by clicking on these links.

**PubMed/Medline Search**

PubMed was developed by the National Center for Biotechnology Information (NCBI) at the National Library of Medicine (NLM), located at the National Institutes of Health (NIH). The PubMed database was developed in conjunction with publishers of biomedical literature as a search tool for accessing literature citations and linking to full-text journal articles at web sites of participating publishers. For more information please refer to the PubMed overview.

**The Lyme Disease Network Medical/Scientific Literature Database**

This database was developed by the Lyme Disease Network of New Jersey (Lymenet), an LDA affiliate.

http://search.lymenet.org/

**Complete Peer Reviewed Articles – Printed with Permission**

Genomes unblock borrelia’s secrets – New Lyme Disease Findings!

Mixed Strains Improve Lyme WB Sensitivity