New Dapsone Study: Breaking Biofilm

Dr. Richard Horowitz, lead-author: Effect of dapsone alone and in combination with intracellular antibiotics against the biofilm form of *B. burgdorferi*

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, sweets 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
**Lyme & Pregnancy Research Study**

The issue of Lyme disease and pregnancy is a serious one, and much more research and education is needed to understand the extent and scope of the problems related to pregnancy and Lyme. The Lyme Disease Association (LDA) is providing information on a study on Lyme and Pregnancy which is led by researchers from the McMasters Midwifery Research Centre in Canada.

The LDA does not recommend or endorse the study but provides the information as a service to those who may want to participate.

Click here for detailed information on the research questionnaire/survey and to participate

Click here for LymeHope update

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**Hydroxychloroquine for Early**
COVID Studies: Participants Needed

The following is a list of studies using Hydroxychloroquine for early COVID disease compiled from ClinicalTrials.gov on April 24, 2020.

Studies using Hydroxy + Azithromycin:

- Rutgers, The State University of New Jersey
  Hydroxy + Zith vs Hydroxy alone vs. no treatment
  PCR + with T 100.6 or more
  Inpatient or outpatient
  Recruiting
- LCMC Health (New Orleans)
  Hydroxy + azith vs. hydroxy alone vs supportive
  Early disease (<7 days of symptoms, PCR +) in 2 groups-
  Early moderate (O2 sat 94+) to severe disease (O2 sat<94)
  Viral load and clinical
  Recruiting

Hydroxy only studies (without azithro):

- ProgenaBiome (CA-based PCR lab)
  Pre-exposure in health care workers
  Hydroxy + vite C + vite D = Zinc vs. no treatment- no doses listed
• Baylor
  Hydroxy only
  Pre-exposure professional healthcare workers
  PCR q wk X 7; weeks, enroll by invitation
• Elizabeth Oelsner, Columbia University
  Hydroxy only; placebo-controlled
  Post-exposure professional to housemates
  Not yet recruiting
• Hackensack Meridian Health
  Hydroxy only, open-label, no placebo
  Pre-exposure professional health care workers
• Washington University School of Medicine
  Hydroxy only- testing 3 different doses
  Pre-exposure; healthcare workers
  Not yet recruiting
• University of Minnesota
  McGill University Health Centre/Research Institute of the McGill University Health Centre
  University of Manitoba
  University of Alberta
  Exposure or early disease <4 days of symptoms
  Hydroxy only vs. Placebo
  Recruiting
• Montefiore Medical Center
  Early disease, confirmed + or suspect
  Hydroxy only
  Not yet recruiting
• Providence Health & Services
  Hydroxy vs. Vitamin C
  Early disease- outpatients, PCR + By invitation
• GeoSentinel Foundation
  Pre-exposure professional health care workers
  Hydroxy vs. placebo
  Not yet recruiting

Thank You Joseph Burrascano, MD for compiling this reference list.
Lyme Campaign Seeks Participants ‘Resilient’ to Lyme & TBD

Mount Sinai researchers have launched a new app in conjunction with the Lyme and Tick-borne Disease Campaign, a project to identify people who seem to be resistant or resilient to ticks and tick-borne diseases including Lyme disease. The Lyme Campaign is seeking thousands of participants, in an effort to find new prevention or treatment strategies for Lyme and tick-borne diseases.

Below are examples of people the Lyme Campaign is interested in:

- Individuals with laboratory test results that indicate an exposure to the bacteria that cause Lyme disease (positive Lyme disease blood test), but who have never been treated with antibiotics and lack typical signs and symptoms of the disease.
- Individuals with high exposure to ticks—such as forestry workers, gardeners, or landscapers—who
either experience bite reactions including pain, swelling, and itching, or those who become immune to ticks and are no longer bitten by bugs.

The campaign will be collaborating with Ben Luft, MD, at the Stony Brook University School of Medicine; Uri Laserson, PhD, Assistant Professor of Genetics and Genomics Sciences at the Icahn School of Medicine at Mount Sinai; and George Church, PhD, and Ting Wu, PhD, Professors of Genetics at Harvard Medical School.

The Lyme Campaign is the first effort of The Resilience Project, which studies individuals who believe they are resilient to a specific disease or health condition. These are people who seem protected against illness or more able than most to recover. These individuals may have been exposed to a germ or have genetic predisposition for a disease—but lack typical signs or symptoms.

Read the Mount Sinai Press Release

Disclaimer: The Lyme Disease Association Inc. (LDA) provides this information as a public service. LDA does not necessarily endorse any of the studies or recommend participation in any studies. Participants need to review the information on the studies and make their own decisions regarding participation.

ClinicalTrials.gov

ClinicalTrials.gov is maintained by the National Library of Medicine (NLM) at the National
Institutes of Health (NIH). Clinical trials are scientific studies conducted to find new treatments and drugs for diseases, as well as ways to prevent, detect, or diagnose diseases. They can show which approaches are most effective and safe for certain illnesses or groups of people. The research in these clinical trials need human participants, as the information cannot be learned from the laboratory or in animals.

When searching ClinicalTrials.gov website for “Lyme” in the “Condition or disease” search box, you can find currently recruiting and completed clinical trials, and can narrow the results to your geographical area.

You will see clinical trials such as those conducted by The Lyme and Tick-Borne Diseases Research Center at the Columbia University Irving Medical Center listed, as well as others.

There are eligibility requirements for clinical trials.

ClinicalTrials.gov does not contain information about all the clinical studies conducted in the United States because not all studies are required by law to be registered (for example, observational studies and trials that do not study a drug, biologic, or device).

Disclaimer: The Lyme Disease Association Inc. (LDA) provides this information as a public service. LDA does not necessarily endorse any of the studies or recommend participation in any studies. Participants need to review the information on the studies and make their own decisions regarding participation.

Click here to find clinical trials on ClinicTrials.gov
Two Columbia Studies Need Participants!

Researchers at Columbia University Lyme and Tick-Borne Diseases Research Center are seeking research study participants for two studies. Women to serve as healthy controls are critical to conducting this first study on metabolomics, and patients with confirmed Lyme disease are needed for the second study on Lyme disease and Disulfiram. Please support these clinical studies.

Dr. Brian Fallon, Investigator

Metabolomics study of Lyme disease: Columbia (Brian Fallon, MD) in collaboration with UCSD:

- Women in Manhattan NY area over next four weeks
- 6-10 healthy women ages 40-60 for controls come to Columbia lab for blood & urine testing, questionnaire, clinical evaluation, sensory testing
- Participants receive $75 & free copies of their bloodwork
- Email Lily Murray for details  lm3448@cumc.columbia.edu

**Lyme patient Disulfiram study:**

- 14 week disulfiram study (Brian Fallon, MD)
- Ages 18-65 with confirmed Lyme disease, persistent fatigue, don’t have other major medical comorbid problems, acquired Lyme within prior 16 years
- All research treatment is provided free of charge
- Inquiries on disulfiram study can be sent to: lymecenter@cumc.columbia.edu or can be made by phone 646-774-7503
- Weblink for this study https://recruit.cumc.columbia.edu/clinical_trial/1661#

For details on these studies and other clinical research opportunities please visit Columbia University, Lyme and Tick-Borne Disease Research Center here.
Hospital Seeks Participants for Powassan Study

Researchers at The Rockefeller University Center for Clinical and Translational Science are conducting a paid study to learn more about the immune systems of people who have been previously infected with Powassan virus. The research team seeks participants who are at least 18 years of age with documented proof of a prior Powassan virus infection. Participation in the study includes up to two outpatient visits to The Rockefeller University Hospital and blood work. Compensation is provided.

If you are interested in participating in this study and would like to learn more, please contact The Rockefeller University Hospital Recruitment Office at 212-327-7722 or send an email to RUCARES@Rockefeller.edu

This study article is provided for informational purposes only. Please do not contact the LDA about the study. Thank you.
Columbia University Research Projects & Columbia Specimen Bank

The Lyme & Tick-Borne Diseases Research Center at Columbia University Medical Center was formed in 2007 by the Lyme Disease Association, Inc. and then Time for Lyme (GLA) in partnership with the Columbia University Board of Trustees. The endowed center was the first of its kind set up to investigate chronic disease. Since that time, many studies have been carried out and published through the Center.

Currently, the Center is looking for research subjects for 3 studies:

**Reducing Chronic Pain in Post-Treatment Lyme Syndrome:** a Brain Imaging and Treatment Study

**Finding Better Tests and Markers for Lyme Disease:** a Study for Patients with Newly Diagnosed Lyme Disease

**Meditation & Kundalini Yoga Breathing** – Do these help to reduce pain & fatigue in patients with chronic lyme disease? Go to http://columbia-lyme.org/research/cr_research.html for details.

Additionally, Columbia has a Specimen Resource Repository housed at Columbia which the LDA contributed funds to that is “committed to serve as a resource for serum and spinal fluid specimens that can be accessed for study both by researchers at Columbia and by researchers throughout the world…. brain, spinal cord, and other tissues from people who have had Lyme disease at some time in their life are collected for current and future investigation at the NYS Psychiatric Institute. People with a history of well-documented Lyme disease, which must include a positive Lyme blood test, should contact us
[Columbia] at 646-774-7503. It is most important that your next of kin or other individual who will be responsible for arrangements after your death be made aware of your wishes, provided with the Columbia Lyme Center contact information, and be informed that they should contact us immediately after your death. Putting aside in a safe place your medical history and laboratory tests is very important as this information is necessary to review before we can conduct the post-mortem investigation. In the event that death has just occurred or is imminent, time is of the essence. If this is the case, please call this emergency number 646-549-8880.


Advanced Laboratory Services Borrelia Test Eval

A Multicenter Study to Evaluate a Borrelia Diagnostic Test in Subjects With Early Stage or Late Stage Lyme Disease

This study is currently recruiting participants. Verified July 2016 by Advanced Laboratory Services, Inc.

Please refer to this study by its ClinicalTrials.gov identifier: NCT02741609

https://clinicaltrials.gov/ct2/show/study/NCT02741609

Purpose

This study will evaluate Advanced Laboratory Services Borrelia diagnostic test by culturing Borrelia spirochetes from human serum in subjects with early or late Lyme
This is an 8 month study. Subjects entering the study will have two blood samples collected one month apart if they have early Lyme disease and one blood sample collected if they have late Lyme disease. Subjects who sign an IRB-approved consent form and meet the inclusion and exclusion criteria will be entered into the study. Subjects will be assigned a subject number upon entry and this number will be retained throughout the study.

<table>
<thead>
<tr>
<th>Study Type:</th>
<th>Interventional</th>
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<tbody>
<tr>
<td>Study Design:</td>
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<td>Official Title:</td>
<td>A Multicenter Study to Evaluate a Borrelia Diagnostic Test in Subjects With Early Stage or Late Stage Lyme Disease</td>
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Further study details as provided by Advanced Laboratory Services, Inc.:

**Primary Outcome Measures:**

- Diagnostic accuracy of the Advanced Laboratory Services, Inc. (ALSI) Borrelia Diagnostic Test (BDT) culture, for positive and negative predictive value, as compared to conventional microbiological methods.
  [ Time Frame: Baseline to 16 weeks ] [ Designated as safety issue: No ]

**Secondary Outcome Measures:**

- Diagnostic accuracy of ALSI culture for early-onset presentation of Lyme disease, as measured by positive and negative predictive value.
  [ Time Frame: Baseline to 16 weeks ] [ Designated as safety issue: No ]
- Diagnostic accuracy of ALSI culture for late-onset presentation of Lyme disease, as measured by positive and negative predictive value.
  [ Time Frame: Baseline to 16 weeks ] [ Designated as safety issue: No ]

| Estimated Enrollment: | 300 |
Study Start Date: April 2016
Estimated Study Completion Date: May 2017
Estimated Primary Completion Date: April 2017 (Final data collection date for primary outcome measure)

Eligibility

<table>
<thead>
<tr>
<th>Ages Eligible for Study:</th>
<th>18 Years and older (Adult, Senior)</th>
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<tr>
<td>Genders Eligible for Study:</td>
<td>Both</td>
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<tr>
<td>Accepts Healthy Volunteers:</td>
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</table>

Criteria

**Inclusion Criteria:**

1. Subject must provide written informed consent prior to the conduct of any study-related procedures.
2. Male or female subjects who are at least 18 years of age.
3. Have early Lyme disease based on the following criteria: Signs, symptoms and clinical history consistent with early stage Lyme disease. Subjects must have a physician-diagnosed erythema migrans (EM) rash and should have systemic symptoms indicative of disseminated infection. Symptoms may include fever, headache, fatigue, myalgias, arthralgias, and stiff neck. Paired acute and convalescent titers will be drawn (first draw at time of initial visit and second draw 4 weeks later) or,
4. Have late Lyme disease based on the following criteria: Signs, symptoms and clinical history consistent with late stage Lyme disease, including but not limited to disseminated rash, arthritis, meningitis, facial palsy, or carditis.
5. Subjects must be willing and have the ability to safely have the required quantity of blood drawn for the study at the discretion of the investigator.
6. Subjects must have blood samples freshly collected (no supplemental frozen samples) and the samples must reach ALSI’s laboratory on a weekday and within 24 hours of being drawn.
Exclusion Criteria:

1. Early Lyme disease: Subjects without an EM rash or do not have symptoms recognized as being associated with Lyme disease.
2. Exposure to antibiotics of any type during the 6 weeks prior to the initial blood sample collection.
3. Immune deficiency significant enough to render serological tests less reliable.
4. The subject is unwilling or unable to safely have the required quantity of blood drawn for this study.
5. Subjects who are not able to understand all of the requirements of the study or unable to give informed consent and/or comply with all aspects of the evaluation.
6. Subjects that have any other condition or situation which, in the opinion of the investigator, would make the subject unsuitable for enrollment or could interfere with the subject participating in and completing the study.
7. Subjects that have undergone testing for Lyme disease within the past year.
8. Subjects that have a prior diagnosis of Lyme disease.

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Contacts

Contact: Phyllis A Mast, MA 484-494-5157 pmast@innovative-cro.com

Locations

<table>
<thead>
<tr>
<th>United States, Delaware</th>
</tr>
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<tbody>
<tr>
<td>Delaware Integrative Medicine</td>
</tr>
<tr>
<td>Georgetown, Delaware, United States, 19947</td>
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<tr>
<td>Contact: Henry Childers IV, MD 302-258-8853</td>
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New Columbia Lyme Treatment Study to Reduce Pain

Reducing Chronic Pain in Post-Treatment Lyme Syndrome: a Brain Imaging and Treatment Study

Background: At least 5-15% of patients with Lyme disease (7,500-45,000 new cases a year) develop Post-treatment Lyme Syndrome (PTLS) – debilitating residual symptoms that last months to years, even after having received antibiotic treatment. Often patients with PTLS experience chronic pain in their muscles or joints or nerves.

Do patients with PTLS benefit from treatment with a medicine that reduces central
pain? Because many PTLS patients have pain that persists despite antibiotics and because we know that medicines which modulate the pain pathways in the brain can help to reduce or eliminate pain, we plan to treat patients with a medicine that is FDA approved for the treatment of pain. This medicine is known as Milnacipran (the trade name is “Savella”); this medicine is not addictive and it has been shown to reduce chronic pain by its multiple actions on pain pathways. All patients in the study will be treated with this FDA approved medicine.

Second, we wish to test whether the pain can be improved even further by adding a medicine which is known to modulate the glutamate transmission involved with pain in the brain. This medicine – D-Cycloserine – is actually an antibiotic, currently FDA approved for the treatment of tuberculosis. Because of its action on glutamate receptors, we are hypothesizing that it will help to decrease pain even further in patients with Lyme-related pain. In order to test this hypothesis, after 6 weeks of being on Milnacipran, all patients will then be given an additional treatment – either D-Cycloserine or a placebo pill (a placebo is a pill that does not contain any active medication.) At the end of 12 weeks, we will then evaluate improvement compared to when the patient started in the study using the same clinical and neuroimaging (fMRI) tests.

Finally, we want to know whether patients with PTLS have over-active central pain circuits in the brain. Because pain is processed through the brain’s pain circuits, we wish to examine whether people suffering from PTLS have hyper-active pain circuits that make them more sensitive to pain than those who have normally-active pain circuits. To do this, we will be comparing patients with PTLS to healthy volunteers by conducting careful neurologic and brain imaging (fMRI) studies.

We hope that this study will provide valuable information about how the brain processes pain signals in PTLS and about whether this treatment approach is effective.

If you are between 18 and 55 years old, have been treated for Lyme disease, and have developed persistent pain post Lyme Infection, you may be eligible!

This study will take place at Columbia University Medical Center: 1051 Riverside Drive, New York, NY. Please contact Ellen Brown at 646-774-8100 or eb3048@cumc.columbia.edu for an initial screening. If you are eligible, all study related procedures and treatment will be conducted at no financial cost to you.
ENROLLMENT START DATE: Feb 2016