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LYME DISEASE FACT SHEET AND PRIORITIES

Lyme Innovation is the continuation of a grassroots effort by the Lyme disease community to address and solve critical challenges. In November 2015, Innovations-X was hosted by the American Academy for the Advancement of Science (AAAS) Science and Technology Policy Fellows. During the “Lyme Science & Solutions: Precision Medicine for Complex Disease” breakout sessions, researchers, clinicians, patients, advocates, and other key stakeholders identified the most pressing priorities in the field of Lyme disease. This process of crowd sourcing priorities was conducted through ignite speeches, round table discussions, and a voting system. In this document, you will read about the top priorities identified in the areas of prevention, diagnostics, treatment, rehabilitation, and precision medicine, as well as general information about Lyme disease.

PREVENTION

- How can we get people to commit to use modes of prevention?
- Given indications in animal studies, how do we study other potential modes of transmission: body fluids? Ingestion?
- How do we educate target populations about post-treatment Lyme disease?
- How do we help educate the providers and the patients about the clinical profile, treatment, prognosis and test options for Lyme disease?

Resources:

- **National Geographic:** Tickborne Diseases: Widespread, Serious, and Taking Us By Surprise, National, Maryn McKenna, August 2015
 - <http://phenomena.nationalgeographic.com/2015/08/31/tickborne-diseases-widespread-serious-and-taking-us-by-surprise/>
- **Tick Encounter Resource Center**
 - <http://www.tickencounter.org/prevention>
- **UMass Amherst, Center for Agriculture, Food, and the Environment**
 - <https://ag.umass.edu/services/tick-borne-disease-diagnostics>

DIAGNOSTICS

- Identify a universal (strain/species) pathogen detection test for all stages of Lyme with high sensitivity and specificity
- How can we develop reliable, highly sensitive and specific tests for active, infectious tick borne diseases, including all stages of Lyme Borreliosis? (ex: economic incentives, validate testing, consider nonhuman primate xenodiagnostic model)
- How can we develop testing for Lyme and tick borne coinfections at all stages of infection?
- How can direct molecular methods be used to identify or develop a broad diagnostic for all tick borne agents to define the underlying cause of all stages of Lyme disease?
- How can we develop novel methodologies for strain specific detection of borrelia in humans?





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- **MYTH: Everyone with Lyme disease gets a telltale bull's-eye rash.**
 - Actually, many never develop a skin rash and those that do may not get a bull's-eye rash. The Centers for Disease Control and Prevention (CDC) estimate that only 70% develop a skin rash (erythema migrans), but this can vary by region. For example, a 2010 study showed that in the state of Maine only 43% of Lyme patients exhibited this particular type of rash. There are a range of symptoms and it is critical that you are alert to all of them.
- **MYTH: If the test is negative, you don't have Lyme.**
 - Not so fast ... The current "gold standard" diagnostic for Lyme disease is a two-tiered blood test requiring a positive ELISA result. The ELISA measures infection-fighting or memory antibodies against *Borrelia burgdorferi*, and it misses up to 60% of acute cases of Lyme when antibodies may not be high enough to detect.
- **Resources:**
 - **Molecular Medicine:** The Pathogenesis of Lyme Neuroborreliosis: From Infection to Inflammation, December 2007
 - <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2148032/>

TREATMENT

- If persister cells are driving Post Treatment Lyme Disease, what is the mechanism?
- Develop eradicating treatment for Lyme infection
- Will a sterilizing compound/regimen prevent Post Treatment Lyme Disease?
- What role do co-infections play in presentation and treatment of Lyme disease?
- **MYTH: Antibiotics cure everyone.**
 - Statistics show that as many as 20% of patients continue to exhibit symptoms even after antibiotic treatment. While there is controversy about the cause of this symptom persistence (e.g., residual bacteria or auto-immune response), for these patients, the suffering continues. As many as a million Americans are estimated to be suffering with this condition, referred to as post-treatment Lyme disease (PTLD).

Resources:

- **Nature:** A new antibiotic kills pathogens without detectable resistance, Ling et al., January 2015
 - <http://www.nature.com/nature/journal/v517/n7535/full/nature14098.html>
- **Scientific American:** Lyme Disease May Linger for 1 in 5 Because of "Persisters", Melinda Wenner Moyer, September 2015
 - <http://www.scientificamerican.com/article/lyme-disease-may-linger-for-1-in-5-because-of-persisters/>
- **Nature, Emerging Microbes and Infections:** Identification of novel activity against *Borrelia burgdorferi* persisters using an FDA approved drug library, July 2014
 - <http://www.nature.com/emi/journal/v3/n7/full/emi201453a.html>
- **PLOS ONE:** Persistence of *Borrelia burgdorferi* in Rhesus Macaques following Antibiotic Treatment of Disseminated Infection, Embers et al, January 2012
 - <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0029914>





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REHABILITATION

- Determine nature of PTLDS/chronic Lyme Disease
- Does fatigue correlate with a Post Treatment Lyme Disease marker?
- What role does inflammation play and how do we address it in treatment?
- How do we rehabilitate the brain and rest of nervous system after injury from Lyme disease?

Resources:

- **The Boston Globe:** New Lyme disease center at Spaulding treats lingering symptoms, October 2015
 - <https://www.bostonglobe.com/metro/2015/10/11/for-lyme-disease-patients-new-approach-aims-ease-residual-effects/Dzq8hZni6BoBiKZ99eq200/story.html>
- **Quality of Life Research:** Post-treatment Lyme disease syndrome symptomatology and the impact on life functioning: is there something here?, John Aucott et al., February 2013
 - <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3548099/>
- **LymeNet:** The Neuropsychiatric Manifestations of Lyme Borreliosis, Brian Fallon et al., Spring 1992
 - <http://library.lymenet.org/domino/file.nsf/bbf2f15334c1f28585256613000317cc/87e8dfed931381b7852567c70012001f?OpenDocument>

PRECISION MEDICINE

- Develop a better model to reflect the complexity and diversity of tick borne diseases (children/adults, psychiatric, strain variation, incorporate social science approach)
- How can precision medicine lead to next-gen diagnostics and treatment? (i.e. how can we replicate what worked for cancer-precision oncology-for Lyme?)
- How can we determine the cause of disease for each patient to guide proper treatment?

Resources:

- **National Institute of Health:** About the Precision Medicine Initiative Cohort Program
 - <https://www.nih.gov/precision-medicine-initiative-cohort-program>
- **The White House:** Precision Medicine Initiative
 - <https://www.whitehouse.gov/precision-medicine>
- **Precision Medicine at UCSF:** The Elements of Precision Medicine (infographic)
 - <http://precisionmedicine.ucsf.edu/elements-precision-medicine>





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GENERAL LYME DISEASE INFORMATION

Lyme disease is a potentially debilitating and sometimes fatalⁱ infection caused by bacteria transmitted through the bite of an infected tick to people and pets.

Statistics

- Lyme disease is the **most common vector-borne infectious disease** in the country
 - **329,000** or more new cases of Lyme disease are diagnosed each year in the U.S., according statistics released in 2015 by the Centers for Disease Control and Prevention (CDC)ⁱⁱ
 - There are many more new cases of Lyme disease than almost any other reportable infectious disease including HIV/AIDS. There are 6 times as many people diagnosed each year with Lyme than HIV in the U.S., according to CDC statistics.ⁱⁱⁱ
 - **Lyme has been reported in all 50 states**, so physicians of every state need to know the symptoms and consider this diagnosis. However, while we are seeing an expansion in the geographic areas inhabited by ticks that carry the bacteria that causes Lyme disease, ticks carrying these bacteria have not been identified in every state at this time.^{iv}
 - The ticks that carry the bacteria which causes Lyme disease have been found in 50% of the counties in the U.S.^v
 - 80 million Americans live in areas of highest risk for Lyme disease^{vi}
 - As a result of the difficulty in diagnosing and treating Lyme disease, at **least 500,000 Americans, and possibly up to one million, suffer from its debilitating later stage symptoms**, according to Bay Area Lyme Foundation estimates^{vii}

National issue

- Awareness of Lyme-infected ticks is critical to increasing early diagnosis of patients in all areas of the country. While CDC accurately highlights that the majority of cases are in the Northeast and Midwest, Lyme can be contracted in the Western states including California, Oregon and Washington.
- Ticks infected with *Borrelia burgdorferi* are widespread in the Bay Area, according to a study released in 2014^{viii} – and another study shows that the risk of contracting Lyme disease in California is year-round too^{ix}.

Ticks

- Ticks often carry more than one version of the bacteria that causes Lyme disease and may also carry other bacteria, viruses and parasites. These separate infections, contracted with the same tick bite, may cause symptoms to vary from person to person, cause challenges with diagnosis and impact which treatments are effective in eradication infections.

Diagnosis

- It is critical to know the symptoms of Lyme disease as a **rash only occurs in approximately 70-80%** of infected persons^x, and fewer get the bull's eye-shaped rash.
- Symptoms of the first stage of Lyme disease include headaches, flu-like symptoms, joint pain, fatigue and *sometimes* a rash that has many different shapes including one which may look like a bull's-eye centered on the tick bite.
- The current "gold standard" diagnostic for Lyme disease **misses up to 60% of cases** of early stage Lyme disease^{xi}.





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- If caught early, most cases of Lyme disease can be treated, but it is commonly misdiagnosed due to lack of awareness and unreliable diagnostic tests. If **not treated promptly**, Lyme may progress to a debilitating stage becoming difficult, or impossible, to cure.
- People with late stage Lyme disease suffer for years with symptoms that can include paralysis, agonizing joint pain, neurological problems, severe headaches, problems with memory, hearing, and vision, inflammation of the brain, and inflammation of the heart. Parents lose their jobs, children suffer in school and families are turned upside down.

Treatment

- Antibiotics do not cure everyone. Approximately **10 to 20% of patients treated for Lyme disease with a recommended 2–4 week course of antibiotics will have lingering symptoms** of fatigue, pain, or joint and muscle pain xii. In some cases it has proven fatal^{xiii}.

West Coast prevalence

- Ticks that carry Lyme disease on the West Coast – the Western blacklegged tick – have been found in all but 2 of the 58 counties (96%) in California.
 - Ticks testing positive for the bacteria have been found in 42 counties (72%)
- While Lyme disease has been reported in every state, there are important differences between Lyme Disease on the West coast and East coast:
 - Throughout the West coast, the tick which transmits Lyme disease is the Western black-legged tick; in the Northeast and Southern parts of the country, it is the blacklegged tick, which is also known as the deer tick.
 - Temperatures vary, so **times of risk vary**. In California, for example, tick season is year round due to its temperate climate^{xiv}, whereas in Massachusetts tick season peaks in the summer months.^{xv}

i <http://www.nbcnews.com/health/three-die-suddenly-rare-lyme-disease-complication-2D11733669>

ii http://wwwnc.cdc.gov/eid/article/21/9/15-0417_article

iii <http://www.cdc.gov/hiv/statistics/basics/ataglance.html>, NIH

iv <http://www.cdc.gov/mmwr/preview/mmwrhtml/ss5710a1.htm>

v <http://jme.oxfordjournals.org/content/early/2016/01/15/jme.tjv237>

vi http://www.cdc.gov/lyme/stats/chartstables/reportedcases_statelocality.html

vii This estimate was developed using data available from the CDC, estimates for under-reporting and data from studies showing the percent of people who do not recover even if treated

viii Salkeld DJ, Cinkovich S, Nieto NC. Tick-borne pathogens in northwestern California, USA [letter]. Emerg Infect Dis [Internet]. 2014 Mar [date cited]. <http://dx.doi.org/10.3201/eid2003.130668>

ix <http://www.sciencedirect.com/science/article/pii/S1877959X14001277>

x Correspondence. The Presenting Manifestations of Lyme Disease and the Outcomes of Treatment. N Engl J Med 2003; 348:2472-2474, June 12, 2003.

xi Rosenfeld , Wang, Schwartz, Wormser, 2005

xii <http://www.cdc.gov/lyme/postLDS/>

xiii <http://www.nbcnews.com/health/three-die-suddenly-rare-lyme-disease-complication-2D11733669>

xiv Ticks and Tick-borne Diseases 2014 <http://doi.org/10.1016/j.ttbdis.2014.05.002>

xv <http://www.ncbi.nlm.nih.gov/pubmed/3687924>

