Proposed amendments to the final report Sept 18, 2021

1. Lyme Disease (*Borrelia burgdorferi*) 2017 CDC Case Definition

https://ndc.services.cdc.gov/case-definitions/lyme-disease-2017/

NOTE: A surveillance case definition is a set of uniform criteria used to define a disease for public health surveillance. Surveillance case definitions enable public health officials to classify and count cases consistently across reporting jurisdictions. Surveillance case definitions are not intended to be used by healthcare providers for making a clinical diagnosis or determining how to meet an individual patient's health needs.

During the course of the Lyme Study Commission, we heard testimony from a number of front-line treating physicians who have treated thousands of Lyme patients and have seen equal numbers of lab test results.

2. Dr. Sam Donta who spent a career studying Lyme disease at BU School of Medicine reported the following:

The following are the essential points I would make regarding "Clinical Diagnosis and Testing" in patients with persisting symptoms, aka "Persistent Lyme disease", "Posttreatment Lyme disease syndrome", "Chronic Lyme disease":

-The diagnosis in such patients is primarily a clinical diagnosis, based on a typical combination of persisting symptoms, and exclusion of other clear diagnostic possibilities.

-Current serology testing, ie two-tiered testing (the screening ELISA test, followed by Western Blot testing only if the ELISA is positive), is insufficiently sensitive in such patients to exclude the diagnosis if the ELISA is negative. The reasons for this are likely that patients with persistent symptoms, as compared to for example patients who have Lyme arthritis-who generate robust immune responses against the causative organisms and who do well with limited courses of antibiotic treatment, mount limited, often muted or no immune responses to B.burgdorferi. This explanation is supported by both the results of animal model studies, including the non-human primate model, and extensive clinical observations, with the primary findings that B.burgdorferi somehow subverts the host immune response such that there is interference with the normal transition of IgM to IgG response. Further support is provided by the clinical observations that Lyme Western Blot testing in many such patients show limited, primarily IgM responses and a few if any IgG responses, and probably more importantly demonstration of one or more immune responses to highly specific B.burgdorferi proteins, ie the 23kd and/or 39kd proteins, in addition to the commonly seen but less specific 41kd protein. And successful treatment of these patients using specific antibiotic regimens for a sufficient duration of time, results in resolution of the IgM responses.

-Based on the above results, it could be recommended that Western Blot testing be directly ordered, bypassing the ELISA test, in patients with possible persisting Lyme disease, its value in potentially supporting the clinical diagnosis, but recognizing that even negative Western Blot tests do not exclude the clinical diagnosis, and the likely basis for empiric antibiotic treatment as the ultimate diagnostic tool.

-If, and until one or more specific markers can be discovered that can more definitively answer the question of whether there is or is not persisting infection by B.burgdorferi, the diagnosis and management of patients with persistent Lyme disease rests on the clinical evaluation and experience of health care providers. **-Dr. Sam Donta**

2. The following chart identifies Western blot bands highly specific to B.burgdorferi as identified by Dr. Sam Donta but is not included with laboratory test results:

Interpretation of the Western blot—More is not necessarily better.

		IgG	IgG	IgM	IgM
Band kDa	Band importance	Ma et al. 2 of 6	CDC 5 of 10	Ma et al 2 of 5	CDC 2 of 3
18	Thought to be specific				
22	Thought to be specific				
23-25	OSP-C highly specific				
28	Not specific				
30	Thought to be specific				
31	OSP-A highly specific				
34	OSP-B highly specific				
37	Thought to be specific				
39	Thought to be specific				
41	Non-specific flagella				
45	Non-specific				
58	Non-specific				
66	Non-specific				
73	Non-specific				
88	Thought to be specific				
93	Thought to be specific				

Engstrom found 2 of 5 bands to be highly sensitive and specific for Lyme disease (Engstrom 1995), while 46 of 66 symptomatic pediatric patients with a history of bulls eye rash and tick bite were negative by CDC criteria (Fawcett 1995 Rheumatology Symposia Abstract #1254.) The CDC criteria are intended only for surveillance purposes, not diagnosis. Many physicians interpret the Western blot based on the number and specificity of the patient's bands. See also (Ma et al. 1989).

3. Note from Dr. Richard Horowitz who has treated over 12,000 Lyme patients:

"Most chronic Lyme patients I have seen do not have CDC + IgG Western blots. They have positive IgM CDC + Western blots and are not necessarily positive by ELISA. I published these results in a study of 200 chronically ill patients we examined who did dapsone combination therapy in our Precision Medicine papers. Please look at table 2 and Figure 3 in the enclosed publication." -Richard Horowitz, MD

Horowitz, R.I.; Freeman, P.R. Precision Medicine: retrospective chart review and data analysis of 200 patients on dapsone combination therapy for chronic Lyme disease/post-treatment Lyme disease syndrome: part 1. International Journal of General Medicine 2019:12 101–119

https://www.dovepress.com/precision-medicine-retrospective-chart-review-and-data-analysis-of-200-peer-reviewed-fulltext-article-IJGM#

"Johns Hopkins published similar results. The reason for the lack of IgG antibodies in many patients is explained in the paper and reflects prior work by Nicole Baumgarth in mice where when borrelia invaded the lymph nodes, and affected B cell and antibody production. Please see the detailed explanation in the paper in Precision Medicine 2, which shows the immune defects we found in the chronic Lyme population." -Richard Horowitz, MD

Clinical Rheumatology **March 2015**

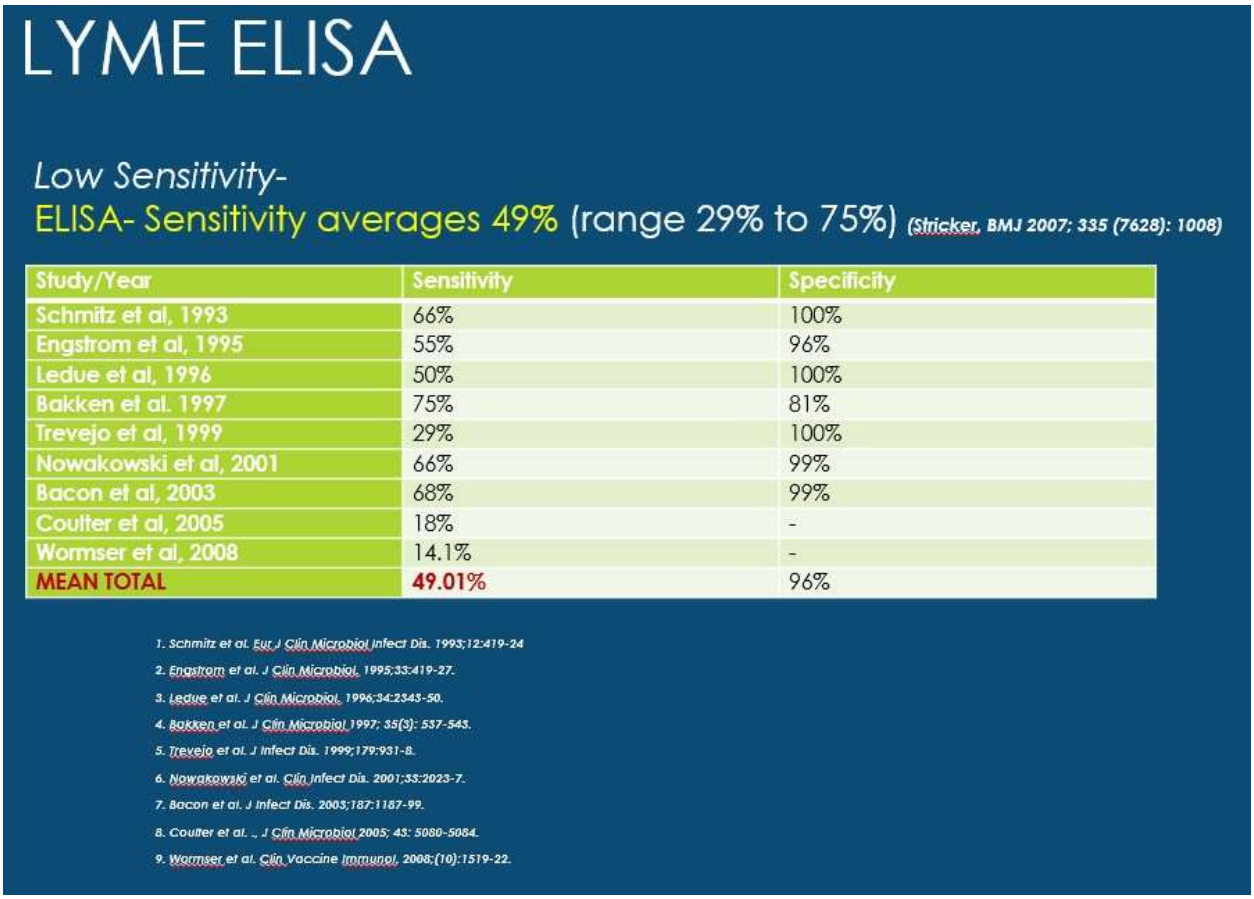
Characteristics of seroconversion and implications for diagnosis of post-treatment Lyme disease syndrome: acute and convalescent serology among a prospective cohort of early Lyme disease patients

Alison W Rebman, Lauren A Crowder, Allison Kirkpatrick, John N Aucott
https://pubmed.ncbi.nlm.nih.gov/24924604/

Excerpt:

"The majority of seropositive individuals on both acute and convalescent serology had a positive IgM western blot and a negative IgG western blot."

4. Nine pier reviewed published studies identifying low sensitivity:

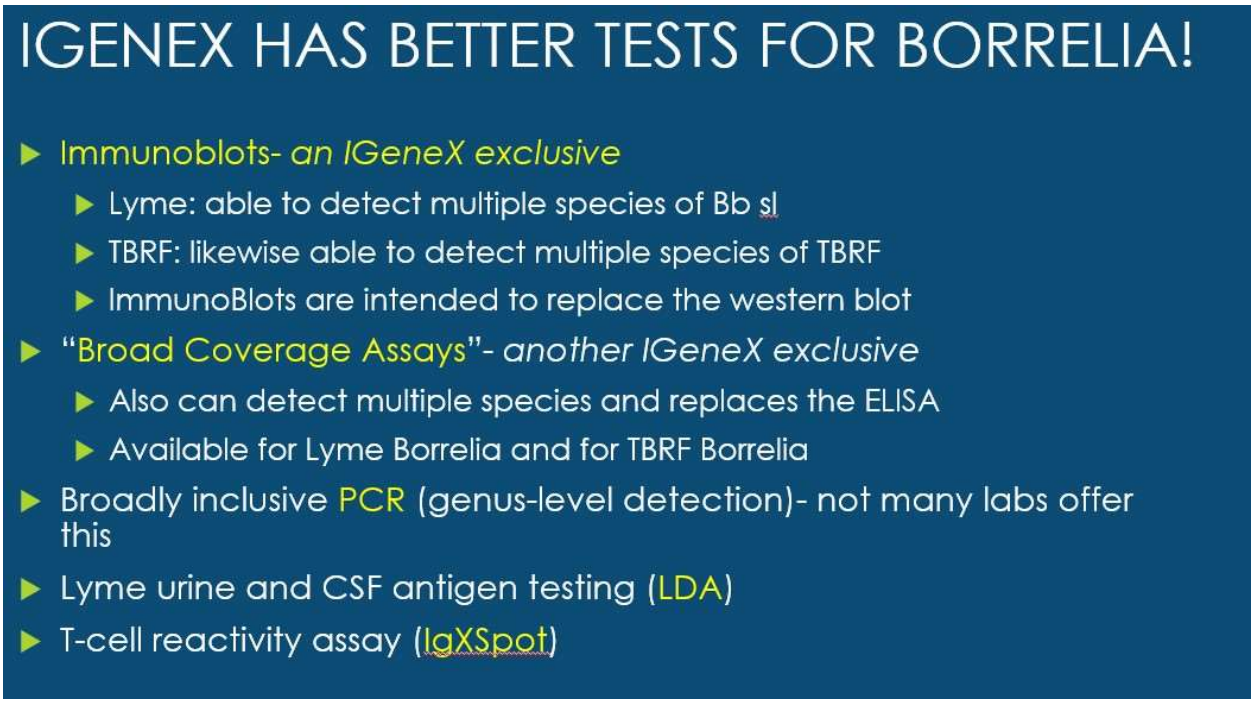


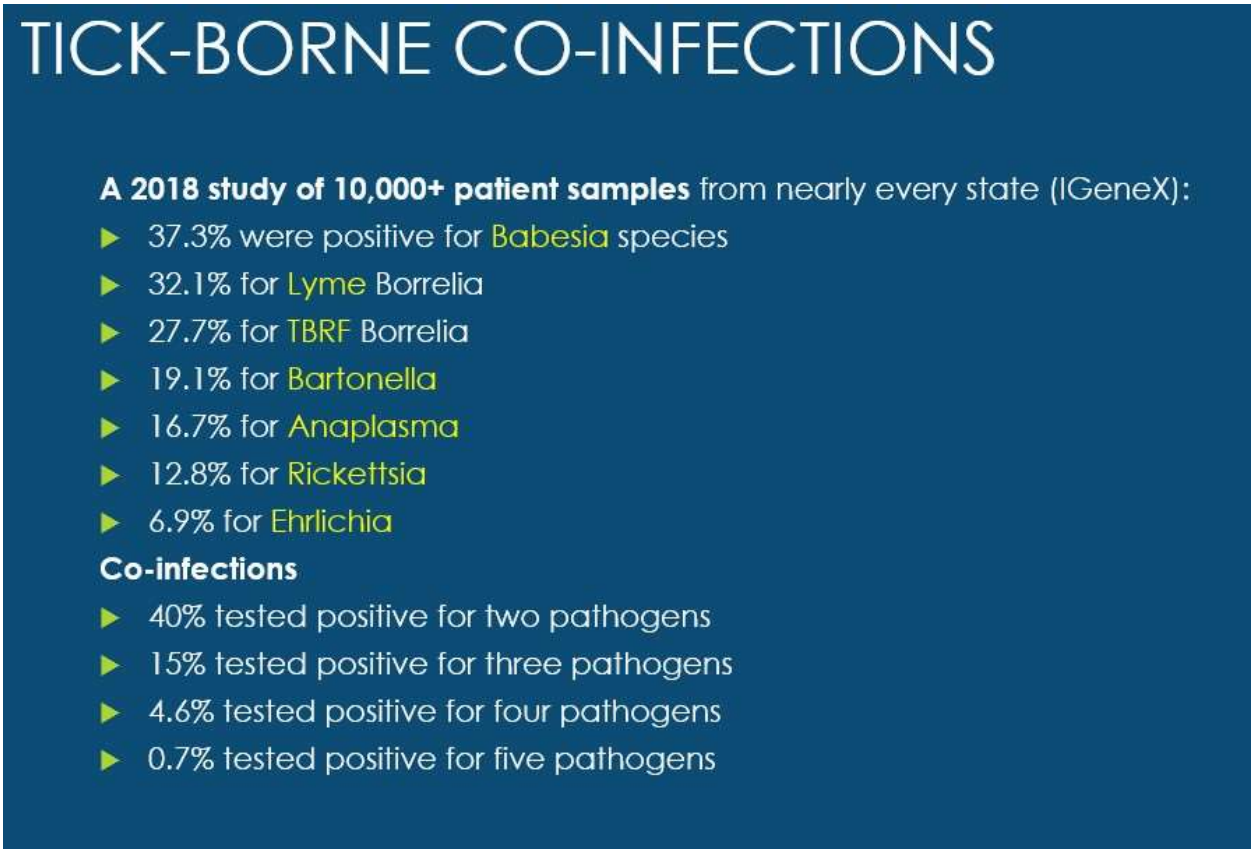
5. Bulls-eye rash has been recorded in less than 50% as reported by the State of Maine Department of Health

State of Maine Department of Health has been tracking incidence of rash and found an average of under 50% for the four years listed below:
2011 42%
http://www.maine.gov/dhhs/mecdc/infectious-disease/epi/vector-borne/lyme/documents/2011-lyme-legislature.pdf
2012 49%
http://www.maine.gov/dhhs/mecdc/infectious-disease/epi/vector-borne/lyme/documents/2012-lyme-legislature.pdf
2013 51%
http://www.maine.gov/dhhs/mecdc/infectious-disease/epi/vector-borne/lyme/documents/2013-lyme-legislature.pdf
2014 57%
http://www.maine.gov/dhhs/mecdc/infectious-disease/epi/vector-borne/lyme/documents/2014-lyme-legislature.pdf

6. Tick-borne Disease testing laboratories were discussed in the Commission

"IgeneX is the most reliable lab for tick-borne infections that I have used in the past 3 decades. Hands down. Quest and LabCorp use one strain of borrelia for testing. IgeneX's Immunoblot uses 8 strains of borrelia and NYS is not an easy state to get approval for testing. They have approved their testing for Lyme for decades (as well as babesia and others). It is only Lyme politics and the IDSA's insistence on how reliable the two-tiered testing is that has muddled reality for certain clinicians." **-Dr Richard Horowitz, Board Certified Internal Medicine**





7. IGeneX has Medicare approval and is CLIA certified:

Medicare Patient Insurance Information
https://igenex.com/wp-content/uploads/Form_MEDICARE_PATIENT_INSURANCE_INFORMATION.pdf

8. Other Tick-Borne Disease Testing Laboratories

GALAXY DIAGNOSTICS, INC. (CLIA-validated molecular and serological assays)
6 Davis Drive, Suite 201
Research Triangle Park, NC 27709
https://www.galaxydx.com/

P: 919-313-9672
F: 919-287-2476
E: contact@galaxydx.com

Milford Molecular Diagnostics (CLIA Certified and approved by the NY Dept of Health)
DNA Sequencing Testing
2044 Bridgeport Ave
Milford, CT 06460
http://dnalymetest.com/

P: 203-878-1438