Minutes of NH subcommittee on Lyme Disease

February 12, 2021

1. Call to order by chairman Marsh
2. Roll call: present- Rep. William Marsh, Rep Mark Pearson, Dr Apara Dave, Tricia Aiston APRN, Dr Frank Hubbell, Dr Abigail Mathewson substituting for Dr. Ben Chan, Carl Tuttle, Christina Dyer, Kathie Fife, Michelle Wagner, Dr. Lynn Durand, Dr Rex Carr.
3. Minutes: the minutes of the January meeting were approved unanimously without corrections.
4. Presentation of Incidence of Lyme Disease in NH: Dr. Mathewson
    a. How is the data gathered?
        i. Data is collected by the state Health Department without state funding but rather funded by the CDC
        ii. Surveillance data
            1. Entomologic data: % of positivity in tested ticks
            2. Human data : from health care provider reports
        iii. Reports from labs which are required to report positive test results
        iv. Reporting from NH health care providers
            1. It has been difficult getting reporting from health care providers
    b. What is the incidence of Lyme Disease in NH?
        i. We are presently at a plateau of incidence in NH
        ii. NH is one of the few high incidence states that tries to follow-up on all positive tests

i.	⁄.2015	⁄.2019	i.Rate
i.Confirmed +	i.1,027	‹.1,105	‹.
i.Probable +	i.344	i.605	⁄.
⁄.total	i.1,371	i.1,710	i.
‹.	‹.	i.	i.128/100,000

xxiii.

    c. Questions/ discussion:
        i. Carl Tuttle: Since testing is felt to under report, isn't this rate underreported?
            1. A: This is a rate based on "case definition" of Lyme Disease. Case Definition should not be considered "clinical definition." Clinical cases are estimated to be 10 X the number of "case definition."
            2. Group discussion: which should we use for our considerations of incidence of Lyme Disease? Conclusion: we should use both definitions and rate.
            3. Dr. Matthewson will provide the CDC link to the study that states the clinical rate is 10X the surveillance case definition rate
        ii. Is there a % of the patients who have mild Lyme Disease an thus never seek medical care and thus are not reported in this data?
            1. A: Dr. Hubbel states that he feels we see the majority of patients who have Lyme Disease.

iii. Tricia Aiston APRN : "I feel that there is a lack of education for the medical providers to know what they are looking for." Thus "patients are not being treated appropriately and indigent patients are more likely to have a missed diagnosis."
iv. Carl Tuttle: stated that he and his family were undiagnosed from their Lyme Disease for 12 years. Thus presenting that our case reporting may be missing many patients.
v. Question: Is Lyme disease a clinical diagnosis (as compared to a lab dx)?
    1. Answer: group consensus that LD is a clinical dx
vi. Dr Durand Question: How does the state handle a case that is report by the health care provider with no EM rash and negative labs but a clinical dx of Lyme Disease
    1. Answer: For the state "surveillance case definition" a patient with no EM rash needs positive labs to be counted as a case definition of Lyme Disease. However, a clinician should be using the clinical definition of Lyme Disease, not the surveillance case definition of lyme disease in their treatment of the patient.
vii. Dr. Matthewson states she "hopes the testing situation will get better" and that Medicare will soon be starting a CME program regarding Lyme disease.
viii. Kathie Fife presented that her test was positive but she was told by the health care provider that "we don't believe the test." Thus it was posited that even with a positive test some patients are not being treated for Lyme Disease. The test involved was from the Igenex Lab and there was discussion as to the reliability of the Igenex lab.

5. Presentation of sensitivity of Two-Tier Test Methodology; powerpoint by Dr. Durand
    a. Article: Evaluation of Two-Tier Serodiagnostic Method for Early Lyme Disease in Clinical Practice; RT Trevejo, J Infect Dz 1999; 179: 931-8.
        i. All pt's had clinical LD based on physician diagnosed EM rash in endemic area
        ii. Sensitivity in acute presentation 32%
        iii. Sensitivity in convalescent time frame: 29%
    b. Article: Two-Year Evaluation of Borrelia burgdorferi Culture and Supplemental Tests for Definitive Diagnosis of Lyme Disease; P Coulter, J Clinical Microbiology 2005, p. 5080-4.
        i. Sensitivity of testing was 75% if used Both serology AND skin PCR
    c. Article: Evaluation of the Serologic Response to Borrelia burgdorferi in Treated Patients with Culture Confirmed Erythema Migrans; ME Aguro-Rosenfield
        i. At days 8 – 14 91% had positive ELISA and/ OR positive WB IgM
        ii. At convalescent 89% had some IgG response but
        iii. Only 22% had positive IgG by CDC criterira
    d. Article: Improved Sensitivity of Lyme Disease Western Blot Prepared with a Mixture of Borrelia burgdorferi strains 297 and B31; JS Shaw; Chronic Diseases-Initernational

i. Igenex lab uses not only the laboratory strain B31 but a clinically obtained strain 297. The data also presents the sensitivity using the CDC criteria as well as the modified criteria set up by the Igenex lab.

Table 2: Comparison of in-house prepared WB with commercially prepared WB (Marblot Test System). A set of 35 sera from patients with confirmed Lyme disease were provided by CDC. CDC also provided Marblot IgM and IgG WB test results. All 35 sera were tested by in-house prepared WB and read by CDC and in-house criteria.

WB Strip Source	Number (percent) positive interpreted with CDC criteria			Number (percent) positive interpreted with in-house criteria			2 tailed Fisher Test**
	IgG	IgM	IgG+IgM	IgG	IgM	IgM+IgG	
Marblot WB tested by the CDC	17 (48.6)**	18 (51.4)*	27 (77.1)	23 (65.7)**	18 (51.4)*	28 (80)	p=0.22
In-house WB tested in-house	22 (62.9)**	27 (77.1)*	31 (88.6)	30 (85.7)**	28 (80)*	34 (97.1)	p<0.1
2 tailed Fisher Test*		p<0.05			p<0.05		

e. Article: Prospective Study for Serologic Tests for Lyme Disease: AC Steere,

Variable	Proportion (%) of patients with positive result, by test(s)			
		Sonicate 2-test approach		
	VlsE C6 peptide ELISA	ELISA and Western blot IgM	ELISA and Western blot IgG	ELISA and Western blot IgM or IgG
Patients with Lyme disease				
Skin infection (stage 1)				
Erythema migrans without evidence of disseminated disease				
Acute	7/36 (19)	4/36 (11)[a]	2/36 (6)[b]	6/36 (17)
Convalescent, after antibiotics	17/36 (47)	14/36 (39)[a]	6/36 (17)[b]	19/36 (53)
Erythema migrans with evidence of disseminated disease[c]				
Acute phase	15/40 (38)	15/40 (38)[a]	6/40 (15)[b]	17/40 (43)
Convalescent phase (after receipt of antibiotics)	25/40 (63)	28/40 (70)[a]	8/40 (20)[b]	30/40 (75)
Disseminated infection (stage 2)				
Acute neurologic or cardiac involvement[d]	13/13 (100)	11/13 (85)	11/13 (85)	13/13 (100)
Persistent infection (stage 3)				
Arthritis or chronic neurologic involvement[e]	31/31 (100)	7/31 (23)	31/31 (100)	31/31 (100)
Post–Lyme disease symptoms	6/14 (43)	7/14 (50)	5/14 (36)	10/14 (71)
Patients with another illness				
And previous Lyme disease	9/14 (64)	1/14 (7)	10/14 (71)	11/14 (79)
Not Lyme disease[f]	1/75 (1)	0	0	0
Healthy subjects				
Area of Lyme disease endemicity	4/86 (5)	1/86 (1)	1/86 (1)	2/86 (2)
Area in which Lyme disease is not endemic	1/50 (2)	0	0	0

Thus showing that:

- Acute pt's with EM and no disseminated disease test sensitivity 17%

- Pt's with EM and with disseminated dz test sensitivity 43%
- Pt's with neurologic or cardiac dz test sensitivity 100%
- Convalescent after abx's test sensitivity 53%
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f. Article: The Accuracy of Diagnostic Terst for Lyme Disease in Humans, A Systematic Review and Meta-Analysis of North American Research; L Weddell, PlosOne, 2016.
   i. Sensitivity for stage 1 dz: 46.3%
   ii. Stage 2: 89.7%
   iii. Stage 3: 99.4%
   iv. Specificity 98.3 – 99.9%

Sensitivity/specificity of commercial two tier testing for convalescent/late stage Lyme disease in the US*

Study/Year	Patients/Controls	Sensitivity	Specificity
Schmitz (1993)	25/28	66%	100%
Engstrom (1995)	55/159†	55%	96%
Ledue (1996)	41/53	44%	100%
Tilton (1997)	23/23	45%	100%
Trevejo (1999)	74/38	29%	100%
Bacon (2003)	106/559	67%	99%
Binnicker (2008)	35/5	49%	100%
Steere (2008)	76/86††	18%	99%
TOTAL	435/951	46%	99%

*Limited to studies from the US that included negative controls; †Non-commercial ELISA and Western blot; ††Non-commercial ELISA

   v.

g. Reference to LymeDisease.org October 9, 2014 article: Two-Tiered Testing for Lyme Disease – No better than a Coin Toss. Time for a Change.
h. Discussion:
   i. Dr Hubbell pointed out that many of the studies are quite dated. Dr. Durand concurred but stated that the test methodology and CDC Two-Tier Methodology guidelines date from the 1990s. Dr. Durand pointed out that the meta-analysis is published in 2016 and he will research newer evaluations of the Two-Tier test methodology sensitivity.
   ii.

6. General Discussions
   a. Test and Treatment Guidelines

i. Dr. Matthewson states the IDSA (Infectious Disease Society of America) has new guidelines. She will provide these to the Committee
ii. Dr. Durand pointed out that the ILADS (International Lyme and Associated Disease Society) also has guidelines. He will provide these as well.
iii. Carl Tuttle presented his personal situation involving very serious chronic persistent lyme disease that was undiagnosed and untreated and has devastated his own health as well as that of his family.
iv. Dr. Carr presented that the testing can be negative in chronic patients as well
v. Kathie Fife suggested a case report of Lyme Disease as an etiology of Alzheimer's Disease

7. Public Comments
    a. Sandy Picard APRN , from Maine, has a Not for Profit organization
    b. Related her personal experience where routine labs for lyme disease were negative but eventually were positive at Igenex Labs and Vibrant America Labs.
    c. She stated she would love to have Maine and NH working together on this issue
8. Other Business
    a. Carl Tuttle pointed out that he has sent out 9 emails with suggested topis for discussion
        i. Related to among others the harm of false negative ELISA tests
        ii. And comments from many patients with lyme disease
        iii. And a list of reference.
    b. Kathie Fife asked about other speakers eg representatives from the Igenex lab and from the Galaxy Lab
9. Next meeting: March 26, 2021 at 9AM by zoom
10. Adjourn 10:51 AM