Chart copy

Kenneth B. Liegner, M.D., P.C.
& Associates
Internal & Critical Care Medicine
Lyme Borreliosis & Related Disorders
592 Route 22 - Suite 1B
Pawling, New York 12564
Ph: 845 493-0274
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November 23, 2011

Lyle R. Petersen, M.D., Ph.D.
Director
Centers for Disease Control
and Prevention
National Center for Emerging and
Zoonotic Infectious Diseases
Division of Vector-borne Diseases
3150 Rampart Road
Fort Collins, Colorado 80521

Dear Dr. Petersen:

Thank you for your nice letter of July 1st concerning the case of Jennifer Lilly, which I presume was forwarded to you by Dr. Frieden's office.

I understand the issues of test design and weighing sensitivity vs. specificity and cost/benefit analyses of mass testing including utility of screening tests followed by tests of higher specificity (and cost).

I have no problem whatsoever with use of CDC clinical case definitions and CDC laboratory definitions of a case of Lyme disease for epidemiologic surveillance purposes. I think it is just fine, for tracking cases over time and from one locale to another and knowing unequivocally that a "case" is a "case".

I *do* have a problem with the *misuse* of CDC surveillance case definitions (whether clinical or laboratory) as the *sole* basis of a diagnosis of Lyme disease and the implication that failure to satisfy CDC case definitions essentially excludes the possibility of Lyme disease for clinical purposes and (importantly) for insurance company reimbursement to the patients for necessary care.

I was heartened to see that the statement has returned to the CDC web-site concerning Lyme disease (which I believe had been absent for a period of time): "This surveillance case definition was developed for national reporting of Lyme disease; it is not intended to be used in clinical diagnosis". Having this statement prominently on CDC's web-site is *extremely* important.

It is my impression that persons with Lyme disease satisfying the surveillance case definition may comprise only 5% or less of persons who actually have Lyme disease. An inkling of this comes from Dr. Fallon who sought candidates for his NINDS study of chronic Lyme disease. Only 1 out of 100 candidates (many of whom had very good clinical histories of Lyme disease with history of EM rash etc.) had positive ELISA and fully diagnostic IgG Western blots which were required to satisfy the entry criteria for the study.

Also, my work with Drs. Garon and Dorward where CDC had forwarded frozen samples of urine from patients I was working with in the early 1990s and tested them with their Rocky Mountain Labororatory Lyme antigen capture assay (detecting membranous blebs shed by the Lyme organism using an immunogold label and electron microscopy) found a large number of persons testing positive on direct detection who were seronegative(**Dorward DW, Schwan TG, Garon CF. Immmune Capture and Detection of Borrelia burgdorferi Antigens in Urine, Blood, or Tissues from Infected Ticks, Mice, Dogs, and Humans. J Clin Microbiol 1991;29:1162-1170 & Liegner KB, Garon C, Dorward D. Lyme borreliosis (LB) studied with the Rocky Mountain Laboratory (RML) antigen capture assay in urine [abstract 18]. Program and abstracts of the Fifth International Conference on Lyme Borreliosis, Arlington, VA, May 30-June2, 1992. Bethesda, MD: Federation of American Societies for Experimental Biology, 1992).**

Additionally, the fortuitous access that I had for my patient's CSFs to be studied at the research lab of Dr. Dattwyler where application of CDC-funded research assays disclosed that 62% of the specimens tested positive on one or more of the advanced research assays (Osp A or Osp C antigen capture and IgG and IgM borrelia-specific assays) whereas only 2% tested positive on standard antibody assays in CSF. These assays were developed by first-class researchers (Dr. Pat Coyle and Dr. Steve Schutzer) [**Coyle PK, Deng Z, Schutzer SE, Belman AL, Benach J, Krupp L, Luft B. Detection of *Borrelia burgdorferi* antigens in cerebrospinal fluid. Neurology 1993;43:1093-1097 & Schutzer SE, Coyle PK, Belman AL, Golightly MG, Drulle J. Sequestration of antibody to *Borrelia burgdorferi* in immune complexes in seronegative Lyme**

disease. Lancet 1990;335:312-315]. I presented this information before the Infectious Diseases Society of America Lyme Disease Review Panel, July 30, 2009 in Washington, D.C. There is a link to this presentation available on the ILADS web-site if you care to view it(www.ILADS.org).

Jennifer Lilly's case is but one of many individuals where the two-tiered method fails them and where widespread ignorance on the part of physicians and over-reliance on dogma (e.g. that if a person has Lyme disease they will invariably test positive on two-tier testing) has resulted in harm and irreversible injury. Accompanying please see reports of Jennifer's MRIs which show the evolution of white matter disease. These lesions apparently developed following use of steroids for a missed diagnosis of Lyme disease which should never have happened. We do not have a baseline study prior to her illness. She has not had lumbar puncture for CSF examination so I suppose it is within the range of possibility that she has unrelated co-incidental multiple sclerosis but I highly doubt this. Jennifer, a highly educated highly capable person accustomed to supervising many individuals in a large department providing mental health services, has been forced by her illness and compromised functioning to resort to disability despite my best efforts thus far (see MRI report[Jennifer has authorized me to disclose this information]).

I have been privileged to get to know and work with many fine individuals and scientists at CDC (I'd been invited out to your campus in the mid-1990s). The amazing work done by Drs. Gilmore and Livengood at CDC demonstrates the complexity of the Lyme organism with its propensity for intracellular sequestration in neurons and supporting cells and its ability *in vitro* to evade destruction by the best and most potent antibiotics presently available to mankind (**Livengood JA, Gilmore RD Jr. Invasion of human neuronal and glial cells by an infectious strain of *Borrelia burgdorferi*. Microbes and Infection 2006;8(14-15):2832-40**).

I would hope that you would use of your good offices to influence the Infectious Diseases Society of America to modify in a constructive way, what has so far been an intransigent position in regard to the existence of seronegative Lyme disease and the possibility of chronic persistent infection by borreliae despite application of antibiotics. It was CDC, Fort Collins, after all, which grew the Lyme organism from the CSF of my patient Vicki Logan following intensive antibiotic treatment (**Liegner KB, Rosenkilde CE, Campbell GL, Quan TJ, Dennis DT. Culture-confirmed treatment failure of cefotaxime and minocycline in a case of Lyme meningoencephalomyelitis in the United States [abstract].**

Programs and abstracts of the Fifth International Conference on Lyme Borreliosis, Arlington, VA, May 30-June 2, 1992. Bethesda,MD: Federation of American Societies for Experimental Biology; 1992:A11).

I urge you at CDC to continue to strive to "serve and protect" the American populace and to take the information I have provided to you as a "frontline" treating clinician into account in the policies and procedures you adopt, which so greatly affect the health of the American people and people around the globe.

Very truly yours & best regards,

Kenneth B. Liegner, M.D.

Member, Treatment Panel, N.I.H. State-of-the-Art Conference on Lyme Disease, March 1991, Bethesda, MD.

Co-Chair, Treatment Poster Discussion Section, Fifth International Conference on Lyme Borreliosis, May/June 1992, Arlington, VA.

Participant, N.I.A.I.D. Consultations on Chronic Lyme Disease, February & October, 1994, Rockville, MD.

Member, Program Committee, 7th International Conference on Lyme Borreliosis, San Francisco, CA., Spring 1996.

Presenter to Infectious Diseases Society of America Lyme Disease Review Panel, July 30, 2009, Washington, D.C.

KBL/ik
Encl.
cc: Jennifer Lilly
Ben Beard CDC, Fort Collins
Thomas F. Frieden, M.D., M.P.H., Director, CDC, Atlanta
Beth P. Bell, M.D., M.P.H., Director, NCEZID, Atlanta
Barbara J.B. Johnson, Ph.D. CDC DVBD, Fort Collins, CO
Eileen Kunkoski, RN & Barbara A. Brookmyer,M.D.,M.P.H.
Frederick County Health Department

Jennifer Lilly ***remains*** seronegative by ELISA despite exhibiting ***fully diagnostic*** IgM and IgG Lyme Western blots at the highly regarded Lyme Immunology Lab at SUNY Stony Brook. As you know, Western blots have greater specificity than the screening ELISA. Furthermore, her history alone should have been sufficient to make a diagnosis and provide her with treatment early on. We have seen other patients with negative ELISAs but fully diagnostic IgG or IgM Lyme Western blots (or both) at Stony Brook.

CDC and State Departments of Health and educators of medical students as well as educators of post-graduate physicians ***must*** do a better job of teaching physicians about Lyme disease and must re-emphasize the importance of clinical evaluation of the patient including detailed history and physical examination and that current methods of testing **cannot always be relied upon**.

CDC should abandon their recommendations for two-tier testing in favor of concurrent ELISA and Western blot testing. Commercial laboratories more concerned with the bugaboo of false positive results have set their cut-offs high so as to avoid this, while at the same time guaranteeing frequent false negative results, consigning patients to needless suffering, as in Jennifer Lilly's case. This applies to both ELISA and Western blot methods. Furthermore, commercial laboratories fail to either test for or report CDC-nonspecific bands on either IgG or IgM blots. Testing for and reporting such bands can provide the clinician with important information. Given the current state of the art of testing, Lyme Western blotting, imperfect as it is, remains an extremely important component of laboratory evaluation of persons who may have Lyme disease.

Jennifer Lilly has written her own comments for you at the Frederick County DOH and CDC which she has asked me to convey along with my letter (copy enclosed).

Very truly yours,

Kenneth B. Liegner, M.D.

Member, Treatment Panel, N.I.H. State-of-the-Art Conference on Lyme Disease, March 1991, Bethesda, MD.

Co-Chair, Treatment Poster Discussion Section, Fifth International Conference on Lyme Borreliosis, May/June 1992, Arlington, VA.

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Presenter to Infectious Diseases Society of America Lyme Disease Review Panel, July 30, 2009, Washington, D.C.

KBL/ik
cc: Thomas F. Frieden, M.D., M.P.H., Director, CDC, Atlanta
Beth P. Bell, M.D., M.P.H., Director, NCEZID, Atlanta
Barbara J.B. Johnson, Ph.D. CDC DVBD, Fort Collins, CO

Encl.

Chart Copy

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March 28, 2011

Frederick County Health Department
350 Montevue Lane
Frederick, Maryland 21702
ATT: Eileen Kunkoski, RN
& Barbara A. Brookmyer, M.D.,M.P.H.

Dear Nurse Kunkoski and Dr. Brookmyer:

We received your Lyme disease report form request concerning Jennifer Lilly, which we return completed. I apologize for the delay in my response.

This young woman gave, to the half dozen or so physicians she encountered over the past 3 years, an unequivocal history of an attached tick occurring in southwestern New Jersey followed by an eruption classic for erythema migrans. Within a few weeks she became acutely ill and presented to an emergency room with fever and severe headache, giving the same history to the emergency room staff. Spinal fluid examination did not reveal pleocytosis and tests for Lyme disease were negative and she received no specific diagnosis and no antibiotic treatment. She was subsequently treated by a neurologist with a course of steroids to control her headache.

She has evolved complex multi-system symptoms which have very significantly impaired her quality of life, interfered with her functioning and caused avoidable suffering. She was repeatedly told she ***could*** not and ***did*** not have Lyme disease because her screening tests for Lyme disease were negative.

There remains a huge gap between the reality of Lyme disease as experienced by patients and simplistic notions about it held widely by physicians. Part of this is due to specious teachings about the illness and the reliability of testing. This includes the two-tier approach, which while it may serve reasonably well in H.I.V. is inappropriate in Lyme disease due to the insensitivity of the screening ELISA. Nonetheless, CDC holds out this sequence of testing as the preferred algorithm and rank and file physicians have been led to believe with a negative ELISA, Western blotting is unnecessary.

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Lyme Borreliosis & Related Disorders
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Ph: 845 493-0274
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December 8, 2011

Ron Rosenberg, ScD
Associate Director for Science
Centers for Disease Control
and Prevention
National Center for Emerging and
Zoonotic Infectious Diseases
Division of Vector-borne Diseases
3150 Rampart Road
Fort Collins, Colorado 80521

Dear Dr.Rosenberg:

Thank you for yesterday's note which I received this morning by FEDEX.

I am glad that you at CDC recognize the dilemmas posed for all of us in diagnosis and treatment of Lyme disease (not to mention other tick-transmissible infections that can be present with or without Lyme disease).

I am glad CDC is encouraging development of improved diagnostic methods and is working on educational programs to more fully educate healthcare providers about the complexities of Lyme disease. I encourage you to incorporate discussion of the *bona fide* problems of seronegativity and chronic persistent infection in your educational materials.

Although sometimes straightforward, in my experience Lyme disease can be extremely challenging to diagnose as well as treat.

I wish you "Godspeed" in achieving your stated objectives.

Very truly yours,

Kenneth B. Liegner, M.D.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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File

July 1, 2011

Kenneth B. Liegner, M.D., P.C.
Internal & Critical Care Medicine
Lyme Borreliosis & Related Disorders
592 Route 22, Suite 1B
Pawling, New York 12564

Dear Dr. Liegner:

Thank you for sending a copy of your letter to the Fredrick County Health Department regarding your patient, Jennifer Lilly. I wish Ms. Lilly a speedy recovery under your care.

As you know, laboratory testing algorithms are derived to balance the often opposing characteristics of test sensitivity, specificity, objectivity, and cost. I appreciate your sharing your experience, and we will keep this information on file for future reference in relation to testing issues.

Sincerely,

Lyle R. Petersen, MD, MPH
Director

7/12/11 Copy mailed to pt Dr

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Centers for Disease Control
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December 7, 2011

Kenneth Liegner, M.D., P.C.
Internal & Critical Care Medicine
Lyme Borreliosis & Related Disorders
592 Route 22, Suite 1B
Pawling, New York 12564

Dear Dr. Liegner:

Thank you for your letter sharing your experience as a "frontline treating clinician" and for your concerns about Lyme disease diagnostic testing. CDC recognizes the threat that Lyme disease poses to public health in the U.S. and is working to improve early and accurate diagnosis and treatment.

To this end, we are developing an educational program for frontline healthcare providers to improve diagnosis and treatment. Additionally, we are workingwith industry and federal partners to make diagnostic testing simpler and more objective.

We are sorry to hear of the ill health of Ms. Lilly and wish her the very best under your care.

Sincerely,

Ron Rosenberg, ScD
Associate Director for Science