Request for Correction of Factual Error in IDSA/AAN/ACR 2020 Guidelines for Prevention, Diagnosis and Treatment of Lyme Disease

October 18th, 2021

Via U.S. Postal Service and Email

Recipients

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Infectious Diseases Society of America
Officers, Directors, Standards and Practice Guidelines Committee

American Academy of Neurology
Officers, Directors, Guidelines Subcommittee

American College of Rheumatology
Officers, Directors, Clinical Practice Guidelines Subcommittee

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Dear Editors, Directors, Officers and Authors:

We are writing to request correction of a statement in the Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA), American Academy of Neurology (AAN), and American College of Rheumatology (ACR): 2020 Guidelines for the Prevention, Diagnosis and Treatment of Lyme Disease which will cause misdiagnosis and harm to pregnant women and children who are congenitally infected. Correction of this error is vital and warrants an expedited review and notice of correction.

Page e12 of the Guidelines "Treatment of Lyme Disease" section states:

> *"To date, Lyme disease in pregnancy has not been found to result in congenital infection or a syndrome of congenital abnormalities, and no additional treatment or monitoring of the mother or infant is recommended beyond the standard of care."*

The statement *"To date, Lyme disease in pregnancy has not been found to result in congenital infection"* is not true.

It is well established that Borrelia spp. can be transmitted in utero from mother to fetus, resulting in congenital infection of the newborn.

Evidence for Congenital Lyme Disease

Transmission of B. burgdorferi from mother to fetus in humans has been documented with Borrelia spirochetes identified in fetal tissues/and or placenta by culture, immunohistochemistry, indirect immunofluorescence, PCR and microscopy.[1]

The first case report of transplacental transmission of *B. burgdorferi* was published in 1985 about a pregnant woman with Lyme disease who delivered an infant with a congenital heart defect who died shortly after birth. Histological examination of fetal tissues at autopsy revealed *B. burgdorferi* spirochetes in the spleen, kidneys and bone marrow.[2]

Also in 1985, the Centers for Disease Control and Prevention (CDC) reported an investigation of Lyme disease and pregnancy. Adverse outcomes, including intrauterine fetal demise, prematurity, and developmental delay with cortical blindness occurred in 5 of the 19 (26%) of the pregnancies.[3]

Both CDC and the National Institutes of Health (NIH) have acknowledged maternal-fetal transmission of Lyme disease in their recent publications[4], and NIH has issued several notices of special interest to encourage research in this field[5]. The HHS Tickborne Disease Working Group has noted this mode of transmission and the health burden it imposes on women and children in its 2018 and 2020 Reports to Congress.

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[1] Appendix A, References 1 – 32

[2] Maternal-fetal transmission of the Lyme disease spirochete, Borrelia burgdorferi. Schlesinger PA, Duray PH, Burke BA, Steere AC, Stillman MT. Ann Intern Med 1985

[3] Lyme Disease and Cases Occurring during Pregnancy. MMWR Weekly, June 28, 1985. 34(25);376-8,383-4

[4] Pregnancy and Lyme Disease, CDC 2020, Lyme Disease: The Facts, The Challenges, NIH 2008

[5] NOT-HD-19-021: Advancing the Understanding, Prevention, and Management of Infections Transmitted from Women to their Infants, NOT-EB-21-001: Small Business Initiatives for Innovative Diagnostic Technology for Improving Outcomes for Maternal Health

While no *singular "syndrome of congenital abnormalities"* exists, multiple studies demonstrate links between Lyme disease during pregnancy and adverse birth outcomes.

The following articles provide evidence of congenital infection with Lyme disease and adverse pregnancy outcomes in treated and untreated patients. Additional references are included in Appendix A.

An Overview of Tickborne Infections in Pregnancy and Outcomes in the Newborn: The Need for Prospective Studies

Lambert JS (2020). Front. Med. 7:72. doi: 10.3389/fmed.2020.00072

> *"Pregnant women represent the single largest vulnerable population in society. Infections in this group not only impact the mother but have the added gravity of impacting the unborn fetus during the most fragile time of human development and can result in catastrophic lifelong changes in the unborn and also intra uterine death."*

A systematic review of the impact of gestational Lyme disease in humans on the fetus and newborn

Waddell LA, Greig J, Lindsay LR, Hinckley AF, Ogden NH. PLoS One. 2018 Nov 12;13(11):e0207067. doi: 10.1371/journal.pone.0207067. PMID: 30419059

> *In this review article, "adverse outcomes" of pregnancy were noted in 11% of pregnant women diagnosed with Lyme disease and treated with IV antibiotics, and 50% of the pregnant women who were not treated.*

Course and Outcome of Erythema Migrans in Pregnant Women

Maraspin V, Lusa L, Blejec T, Ružić-Sabljić E, Pohar Perme M, Strle F. J Clin Med. 2020 Jul 24;9(8):2364. doi: 10.3390

> *This study included 304 pregnant women with EM who received 14 days of antibiotic treatment. The outcome of pregnancy was unfavorable in 42/304 (13.8%) patients, appraised by fetal death, pre-term birth and offspring malformations.*

Maternal Lyme borreliosis and pregnancy outcome

Lakos A, Solymosi N. Int J Infect Dis. 2010 Jun;14(6): PMID: 19926325

> *"Adverse outcomes were seen in 8/66 (12.1%) parentally treated women, 6/19 (31.6%) orally treated women, and 6/10 (60%) untreated women."*

Studies by Guidelines Authors Provide Additional Evidence

Several authors of the IDSA/AAN/ACR 2020 guidelines co-authored studies that clearly contradict what they've written in the Guidelines, and which address the issue of intrauterine transmission and fetal abnormalities head-on.

Allen C. Steere

Lyme disease during pregnancy

Markowitz L, Steere A, Benach J, Slade J, Broome C. JAMA. 255/24 (3394-3396), 1986

> *Nineteen cases of Lyme disease in pregnant women were identified with onset between 1976 and 1984. Thirteen received antibiotic therapy for Lyme disease. Of the 19 pregnancies, five had adverse outcomes, including syndactyly, cortical blindness, intrauterine fetal death, prematurity, and rash in the newborn.*

The spectrum of organ and systems pathology in human Lyme disease

Duray, Paul Harrison; Steere, Allen C. Zentralbl Bakteriol Mikrobiol Hyg A. 1986

> *"The heart of the neonate born to a mother with untreated Lyme disease showed numerous cardiac malformations."*

Clinical pathologic correlations of Lyme disease by stage

Duray, P, Steere, Annals of the New York Academy of Sciences, Vol 539:65-79, 1988

> *"It is clear that B. burgdorferi can be transmitted in the blood of infected pregnant women across the placenta into the fetus. This has now been documented with resultant congenital infections and fetal demise."*

Gary P. Wormser

Treatment of Borrelia burgdorferi infection

Gary P. Wormser. Laboratory Medicine, Volume 21, Issue 5, 1 May 1990, Pages 316-321

> *"The precise risk to the developing fetus of maternal Lyme disease during pregnancy is unknown, although it is well documented that fetal infection can occur and may have deleterious outcomes, including malformations and death."*

Franc Strle

Treatment of erythema migrans in pregnancy

Maraspin V, Cimperman J, Lori-Furlan S, Pleterski-Rigler D, Strle F. Clinical Infectious Diseases 1996; 22, 788-93

> *"During gestation B. burgdorferi may spread transplacentally to the fetus, causing adverse outcome of pregnancy, including various congenital abnormalities, premature birth, and even fetal death."*

Erythema migrans in pregnancy

Maraspin V, Cimperman J, Lotric-Furlan S, Pleterski-Rigler D, Strle F. Wein Klin Wochenschr (1999) 111/22-23:933-940

> *Out of 105 pregnant women with erythema migrans who were treated with antibiotics for 14 days, adverse outcomes were noted in seven cases (11.4%), including six (5.7%) with preterm birth. One of the preterm babies had cardiac abnormalities and two died shortly after birth. Four (3.8%) babies born at term were found to have congenital anomalies.*

John J. Halperin

A perspective on the treatment of Lyme borreliosis

Luft BJ, Gorevic PD, Halperin JJ, Volkman DJ, Dattwyler RJ. Rev Infect Dis. 1989 Sep-Oct;11 Suppl 6:S1518-25. doi: 10.1093/clinids/11.supplement_6.s1518. PMID: 2682965

> *"The aim of treatment of early Lyme disease during pregnancy is not only to treat the infection and prevent long-term sequelae but to eliminate the infection as quickly as possible so as to prevent congenital transmission to the fetus."*

Maria E. Aguero-Rosenfeld

Confirmation of Borrelia burgdorferi spirochetes by polymerase chain reaction in placentas of women with reactive serology for Lyme antibodies

Figueroa R, Bracero LA, Augero-Rosenfeld, M et al. Gynecol Obstet Invest. 1996;41(4):240-3

> *"Sixty placentas of asymptomatic women with ELISA-positive or-equivocal serology for Lyme antibodies during pregnancy were examined for spirochetes using a silver stain. Spirochetes were identified by silver staining in 3 (5%) of the 60 placentas. PCR confirmed B. burgdorferi nucleotide sequences in 2 of the placentas."*

It is disheartening and alarming that the authors of medical guidelines that direct the care of pregnant women with Lyme disease are ignoring their own research to put forward guidelines based on "expert opinion" rather than their own discoveries. Their own work conclusively proves that perinatal transmission of *B. burgdorferi* during pregnancy does occur and may have dire consequences for the pregnant mother and her fetus.

Harm to Mothers, Children and Families

The potential harm to mothers, children, and families from the inaccurate information in the IDSA/AAN/ACR 2020 Lyme guidelines is significant. Providers who rely on the Guidelines will fail to diagnose and treat Lyme disease in pregnancy and fail to recognize the offspring of women with Lyme disease as infants and children at risk. Countless tragic births and fetal losses will result, with a lifetime of harm to the children and their families.

The 2020 Guidelines say that "*no additional treatment or monitoring of the mother or infant is recommended beyond the standard of care*."

Instead, the Guidelines should describe the manifestations of Lyme in pregnancy that the research has uncovered and advise screening and treatment according to the knowledge we have to date.

Requested Actions

The statement on congenital Lyme disease should be fully retracted and replaced with the following:

"Research has shown that Lyme bacteria can cross the placenta, both infecting and causing harm to unborn children.

Women with Lyme disease are more likely to be seronegative, so a negative test at any stage of the disease should not be used to rule out Lyme disease.

Women who are infected with Lyme disease during pregnancy should be treated and monitored throughout pregnancy.

Evaluation of a pregnancy that has been complicated by Lyme disease should include evaluation for coinfections and a pathologic examination of the placenta to detect evidence of spirochetes."

We request an acknowledgement our correspondence has been received and look forward to meeting with representatives of the sponsoring organizations to discuss working together to advance research.

Sincerely,

Isabel Rose, Chair, Mothers Against Lyme
Isabel.Rose@MothersAgainstLyme.org

Concurring Directors and Advisers: Kristina Bauer[1], Chris Fisk[2], Bruce Fries[3,9], Rosalie Greenberg, MD[4], Jane Marke, MD[4,9], Isabel Rose[5], Monte Skall[6], Monica White[7], Ronald Wilson, MD[8]

[1] Texas Lyme Alliance, [2] Lyme Action Network, [3] Patient Centered Care Advocacy Group,[4] Private Practice, Psychiatry, [5] Project Lyme, [6] National Capital Lyme and Tick-Borne Disease Association, [7] Colorado Tick-Borne Disease Awareness Association, [8] ILADS member and retired OBGYN, [9] Co-Founder Mothers Against Lyme

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Appendix A

Additional References on Congenital Transmission of Lyme/TBD

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