

## Evidence for Transplacental Transmission of Lyme disease in Humans and Animals

Evidence for transmission of *Borrelia burgdorferi* in pregnancy, from mother to placenta and/or fetus/neonate/child includes 38 cases of possible or probable congenital Lyme infection and 28 cases of placental infection. In an additional 2 cases, Bb DNA has been identified in human breastmilk.

- 21 cases whereby *Borrelia burgdorferi* or *Borrelia* spp. was identified via autopsy of fetal or neonate tissue.<sup>1-11</sup>
- 1 case of a child who died at age 7 because of cerebral complications of congenital Lyme borreliosis, positive serology at birth and PCR positive placenta.<sup>12</sup>
- 16 cases of live-birth, neonatal infection and adverse outcomes, including two cases where Bb antibodies were identified in the cerebral spinal fluid (CSF) of infected symptomatic neonates.<sup>5,10-23</sup>
- 2 cases of live-birth, Bb identified by PCR in cordblood of infants whose mothers were treated.<sup>23</sup>
- 28 cases whereby Bb has been identified in placenta: 17 cases Bb identified by PCR in placentas of treated pregnant women<sup>9,10,12,23,24</sup> 2 cases Bb identified by PCR in placentas of (treatment not stated) pregnancies.<sup>25</sup> 4 cases Bb identified in placenta by histology/staining/IFA in untreated pregnancies.<sup>5</sup> 5 cases Bb identified in placenta by histology/staining/MoAb in treated pregnancies.<sup>5,11,26,27</sup>
- 2 cases whereby Bb has been identified in breastmilk by PCR of untreated women with EM rash.<sup>28</sup>

In animals, studies have reported transplacental transmission of *Borrelia burgdorferi* under experimental conditions (mice and dogs)<sup>29-32</sup> and in natural populations of mice,<sup>33-35</sup> horses,<sup>36</sup> cows,<sup>37,38</sup> coyotes,<sup>39</sup> and foxes.<sup>40</sup>

The US Centers for Disease Control and Prevention (CDC)<sup>41</sup> and Health Canada<sup>42</sup> currently acknowledge the risk of maternal-fetal transmission of Lyme disease on their respective websites. The UK Royal Society of Obstetricians and Gynecologists lists Lyme disease as one of the infectious organisms which can cross the placenta leading to late intrauterine fetal death and stillbirth.<sup>43</sup> Guidelines issued by the Swiss Society for Infectious Diseases report that transplacental infections with *B. burgdorferi* can be seen in all three trimesters.<sup>44</sup>

The current (8<sup>th</sup>) edition of the authoritative medical reference textbook on congenital infections, *Remington and Klein's Infectious Diseases of the Fetus and Newborn Infant*, includes *Borrelia burgdorferi* as one of several pathogenic microorganisms responsible for infection of the fetus.<sup>45</sup>

Guidelines for the diagnosis and treatment of pregnant women with Lyme disease, diagnostic criteria for infants suspected of congenital infection, and treatment recommendations for both mother and baby were developed by experts from the CDC (1990)<sup>46</sup> and Infectious Diseases Society for Obstetrics and Gynecology (1992 and 2000).<sup>47,48</sup> Currently there are no interim guidelines for the diagnosis and treatment of gestational and congenital Lyme disease, but they are needed.<sup>49</sup>

Publications specifically addressing Lyme disease and pregnancy,<sup>19,50-62</sup> vector-borne infections in pregnancy,<sup>63-67</sup> fetal /congenital infections,<sup>45,68-70</sup> epidemiology of Lyme disease,<sup>71</sup> pathology associated with congenital Lyme,<sup>5,72,73</sup> infectious causes of stillbirth,<sup>74-76</sup> and Lyme disease in general,<sup>77-84</sup> address maternal-fetal transmission of the Lyme disease spirochete and risk of adverse pregnancy outcomes.

## Citations

1. Schlesinger PA, Duray PH, Burke BA, Steere AC, Stillman MT. Maternal-fetal transmission of the Lyme disease spirochete, *Borrelia burgdorferi*. *Ann Intern Med*. 1985;103(1):67-68. doi:10.7326/0003-4819-103-1-67
2. Lavoie PE, Lattner BP, Duray PH, Barbour AG, Johnson RC. Culture Positive Seronegative Transplacental Lyme Borreliosis Infant Mortality A:74. *American Rheumatism Association, 51st Annual Meeting, Scientific Abstracts*. Published online 1987:S50.
3. Macdonald AB. Human fetal borreliosis, toxemia of pregnancy, and fetal death. *Zentralbl Bakteriolog Mikrobiol Hyg A*. 1986;263(1-2):189-200. doi:10.1016/S0176-6724(86)80122-5
4. MacDonald AB, Benach JL, Burgdorfer W. Stillbirth following maternal Lyme disease. *N Y State J Med*. 1987;87(11):615-616.
5. MacDonald AB. Gestational Lyme borreliosis. Implications for the fetus. *Rheumatic Disease Clinics of North America*. 1989;15(4):657-677.
6. Neubert U. Erythema migrans in der Gravidität. *Hautarzt*. 1987;38:182-183.
7. Maraspin V, Cimperman J, Lotric-Furlan S, Pleterski-Rigler D, Strle F. Erythema migrans in pregnancy. *Wein Klin Wochenschr*. 1999;111(22-23):933-940.
8. Weber K, Bratzke HJ, Neubert U, Wilske B, Duray PH. *Borrelia burgdorferi* in a newborn despite oral penicillin for Lyme borreliosis during pregnancy. *Pediatr Infect Dis J*. 1988;7(4):286-289. doi:10.1097/00006454-198804000-00010
9. Horowitz RJ, Yunker LL. Lyme Disease and Pregnancy: Implications of Chronic Infection, PCR Testing, and Prenatal Treatment. In: *16th International Scientific Conference on Lyme Disease & Other Tick-Borne Disorders*. Lyme Disease Foundation; 2003.
10. Hulínská D, Votýpka J, Vaňousová D, et al. Identification of *Anaplasma phagocytophilum* and *Borrelia burgdorferi sensu lato* in patients with erythema migrans. *Folia Microbiol (Praha)*. 2009;54(3):246-256. doi:10.1007/S12223-009-0039-0
11. Hercagova J, Hulinska D, Zivny J, Janovska D. D648 Erythema Migrans during Pregnancy: Study of 35 Women. In: *VII International Congress on Lyme Boreliosis*. ; 1996:172.
12. Spector R, Rummelt V, Folberg R. 1466-27 The Pathology of Ocular Congenital Lyme Borreliosis. In: *Investigative Ophthalmology & Visual Science Annual Meeting*. Vol 34. ; 1993:1001.
13. Markowitz LE, Steere AC, Benach JL, Slade JD, Broome C V. Lyme disease during pregnancy. *JAMA*. 1987;255(24):3394-3396.
14. Lampert F. Infantile multisystem inflammatory disease: another case of a new syndrome. *Eur J Pediatr*. 1986;144(6):593-596. doi:10.1007/BF00496045
15. Volkman DJ, Dattwyler RJ. Immunodiagnosis and Treatment of Lyme Borreliosis. *Med Times*. 1989;117(8):59-71.
16. Horst H. *Borrelia burgdorferi*-Infektionen in der Schwangerschaft. In: Hassler D, ed. *Fortschritte Der Infektiologie: Lyme-Borreliose [Advances in Infectious Disease Management. Lyme Borreliosis]*. MMV Medizin Verlag GmbH München; 1992:85-92.
17. Gasser R, Dusleag J, Reisinger E, et al. A most unusual case of a whole family suffering from late Lyme borreliosis for over 20 years. *Angiology*. 1994;45(1):85-86. doi:10.1177/000331979404500114
18. Trevison G, Stinco G, Cinco M. Neonatal skin lesions due to a spirochetal infection: a case of congenital Lyme borreliosis? *Int J Dermatol*. 1997;36(9):677-699. doi:10.1046/J.1365-4362.1997.00217.X
19. Gardner T. Lyme Disease. In: Remington JS, Klein JO, eds. *Remington and Klein's Infectious Diseases of the Fetus and Newborn Infant*. 5th ed. W.B Saunders Company; 2001:519-641.
20. Lazebnik T, Zal'tsman P. A case of Congenital Neuroborreliosis. *Scientific and Practical Journal of Neurosurgery and Childhood Neurology, St Petersburg, Russia*. Published online 2005.
21. Jones CR, Smith HS, Gibb E, Johnson L. Gestational Lyme Disease Case Studies of 102 Live Births. *LymeTimes*. Published online 2005:36-38.

22. Önk G, Acun C, Kalayci M, Çağavi F, Açıkgöz B, Tanriverdi HA. Gestational lyme disease as a rare cause of congenital hydrocephalus. *Journal of the Turkish German Gynecology Association*. 2005;6(2):156-157. Accessed May 5, 2024. <https://utsouthwestern.elsevierpure.com/en/publications/gestational-lyme-disease-as-a-rare-cause-of-congenital-hydrocephala>
23. Vanousova D, Nemvoca A, Hulinska D, Schmiedbergerova R, Hercagova J. Transplacentární přenos borelií? . *Cesk Dermatol*. 2007;82(4):218.
24. Hulínská D, Votýpka J, Hořejší J. Diseminovaná borrelióza a její průkaz v laboratoři [Disseminated Lyme borreliosis and its laboratory diagnosis]. *Zprávy Epidemiologie A Mikrobiologie*. 2011;20(1):24-26.
25. Figueroa R, Bracero LA, Agüero-Rosenfeld M, Beneck D, Coleman J, Schwartz I. Confirmation of *Borrelia burgdorferi* spirochetes by polymerase chain reaction in placentas of women with reactive serology for Lyme antibodies. *Gynecol Obstet Invest*. 1996;41(4):240-243. doi:10.1159/000292277
26. Burrascano JJ. Failure of Aggressive Antibiotic Therapy to Protect the Placenta From Invasion by *B. Burgdorferi* in a Pregnant Patient with Lyme Borreliosis. In: *Sixth Annual International Science Conference on Lyme Disease and Other Tick-Borne Diseases*. ; 1993.
27. Patmas MA. Persistence of *Borrelia burgdorferi* Despite Antibiotic Treatment. *Journal of Spirochetal and Tick-Borne Diseases*. 1994;1(4):101.
28. Schmidt BL, Aberer E, Stockenhuber C, Klade H, Breier F, Luger A. *Detection of Borrelia Burgdorferi DNA by Polymerase Chain Reaction in the Urine and Breast Milk of Patients with Lyme Borreliosis*.
29. Ubico-Navas S. *Experimental and Epizootiologic Studies of Lyme Disease*. . PhD. Colorado State University; 1992.
30. Altaie S, Mookherjee S, Assian E, Al-Taie F, Nakeeb S, Siddiqui S. Transplacental Transmission of Bb In a Murine Model. In: *10th Annual International Scientific Conference on Lyme Disease & Other Tickborne Disorders, National Institutes of Health*. ; 1997.
31. Gustafson J, Burgess E, Wachal M, Steinberg H. Intrauterine transmission of *Borrelia burgdorferi* in dogs. *Am J Vet Res*. 1993;54(6):882-890.
32. Silver RM, Yang L, Daynes RA, Ware Branch D, Salafia CM, Weis JJ. *Fetal Outcome in Murine Lyme Disease*. Vol 63.; 1995. <http://iai.asm.org/>
33. Wan K, Zhang Z, Wang H, Hou X. [Preliminary investigation on reservoir hosts of *Borrelia burgdorferi* in China]. *Wei Sheng Yan Jiu* . 1999;28(1):7-9.
34. Anderson,' JF, Johnson RC, Magnarelli' LA. *Seasonal Prevalence of Borrelia Burgdorferi in Natural Populations of White-Footed Mice, Peromyscus Leucopus*.; 1987. <http://jcm.asm.org/>
35. Burgess EC, Cleven TD. *Borrelia Burgdorferi Infection in Dairy Cows, Rodents, and Birds from Four Wisconsin Dairy Farms*. Vol 35.; 1993.
36. Burgess E, Gendron-Fitzpatrick A, Mattison M. Foal mortality associated with natural infection of pregnant Mares with *Borrelia burgdorferi*. In: Powell D, ed. *5th Int. Conference Equine Infectious Diseases*. The University Press of Kentucky; 1989:217-220.
37. Burgess E. *Borrelia burgdorferi* infection in Wisconsin horses and cows. *Ann N Y Acad Sci*. 1988;539(1):235-243. doi:10.1111/J.1749-6632.1988.TB31857.X
38. Leibstein M, Khan M, Bushmich S. Evidence for in-utero Transmission of *Borrelia burgdorferi* from Naturally Infected Cows. *Journal of Spirochetal and Tick-borne Diseases*. 1998;5(Fall/Winter):54-62.
39. Burgess EC, Windberg LA. *Borrelia* sp. infection in coyotes, black-tailed jack rabbits and desert cottontails in southern Texas. *J Wildl Dis*. 1989;25(1):47-51. doi:10.7589/0090-3558-25.1.47
40. Gustafson J. *The in Utero and Seminal Transmission of Borrelia Burgdorferi in Canidae*. PhD. The University of Wisconsin Madison; 1993.
41. United States Centers for Disease Control and Prevention. Ticks and Lyme Disease: Pregnancy and Lyme disease. Pregnancy and Lyme Disease. Published January 27, 2020. Accessed April 16, 2024. <https://www.cdc.gov/lyme/resources/toolkit/factsheets/Pregnancy-and-Lyme-Disease-508.pdf>

42. Health Canada. Risks of Getting Lyme Disease: Pregnant People. Lyme Disease Prevention and Risks. Published February 8, 2024. Accessed April 16, 2024. <https://www.canada.ca/en/public-health/services/diseases/lyme-disease/prevention-lyme-disease.html>
43. Royal College of Obstetricians and Gynaecologists. Late Intrauterine Fetal Death and Stillbirth Green-top Guideline No. 55. Published online 2010. Accessed April 28, 2024. <https://www.rcog.org.uk/guidance/browse-all-guidance/green-top-guidelines/late-intrauterine-fetal-death-and-stillbirth-green-top-guideline-no-55/>
44. Evison J, Aebi C, Francioli P, et al. Borréliose de Lyme 3e partie: Prévention, grossesse, états d'immunodéficience, syndrome post- borréliose de Lyme. *Rev Med Suisse*. 2006;2(60):935-940. doi:10.53738/REVMED.2006.2.60.0935
45. Maldonado YA, Nizet V, Klein JO, Remington JS, Wilson CB. Current Concepts of Infections of the Fetus and Newborn Infant. In: Maldonado Y, Wilson CB, Remington JS, Klein JO, Nizet V, eds. *Remington and Klein's Infectious Diseases of the Fetus and Newborn Infant*. 8th edition. Elsevier; 2016:3-23.
46. Moore PS. Fetal Effects from Lyme Disease (3212). In: Buyse ML, ed. *The Birth Defects Encyclopedia*. Blackwell Scientific Publications; 1990:696-697.
47. Williams Christine L., Welch Peter C. Lyme Disease in Pregnancy. In: Mead PB, Hager WD, eds. *Infection Protocols for Obstetrics and Gynecology: Infectious Diseases Society for Obstetrics and Gynecology*. Contemporary Ob/Gyn; Medical Economics Publishing; 1992:56-61.
48. Amstey M. Lyme Disease in Pregnancy. In: Mead PB, Hager WD, Faro S, eds. *Protocols for Infectious Diseases in Obstetrics and Gynecology; Infectious Diseases Society for Obstetrics and Gynecology*. 2nd ed. Blackwell Science Inc.; 2000:105-109.
49. *Tick-Borne Disease Working Group 2022 Report to Congress, 3rd Report.*; 2022. Accessed May 14, 2024. <https://www.hhs.gov/sites/default/files/tbdwg-2022-report-to-congress.pdf>
50. Silver HM. Lyme disease during pregnancy. *Infect Dis Clin North Am*. 1997;11(1):93-97. doi:10.1016/S0891-5520(05)70343-3
51. Alexander JM, Cox SM, Alexander JM. Lyme disease and pregnancy. *Infect Dis Obstet Gynecol*. 1995;3(6):256-261. doi:10.1155/S1064744995000755
52. Schutzer SE, Janniger CK, Schwartz RA. Lyme disease during pregnancy. *Cutis*. 1991;47(4):267-268.
53. Williams C, Strobino B. Lyme Disease Transmission During Pregnancy. *Contemp Ob Gyn*. Published online June 1990:48-54.
54. Cartter ML, Hadler J.I., Gerber M.A., Mofenson L. Lyme Disease and Pregnancy. *Conn Med*. 1989;32(6):341-342.
55. O'Brien J, Martens M. Lyme disease in pregnancy: a New Jersey medical advisory. *MD Advis*. 2014;Winter 7(1):24-27.
56. Elliott DJ, Eppes SC, Klein JD. Teratogen update: Lyme disease. *Teratology*. 2001;64(5):276-281. doi:10.1002/tera.1074
57. Salzman MB, Rubin LG. Lyme Disease During Pregnancy. *Children's Hospital Quarterly*. 1991;3(3):175-177.
58. Edly S. Lyme Disease During Pregnancy. *N J Med*. 1990;87(7):557-560.
59. Smith LJ, Pearlman M, Smith L, Faro S. Lyme disease: A Review with Emphasis on the Pregnant Woman. *Obstet Gynecol Surv*. 1991;46(3):125-130.
60. American Academy of Obstetrics and Gynecology (ACOG) Committee Opinion: Committee on Obstetrics: Maternal and Fetal Medicine. Lyme Disease During Pregnancy. *Int J Gynaecol Obstet*. 1992;39(1):59-60.
61. Sicuranza G, Baker DA. Lyme Disease in Pregnancy. In: Coyle PK, ed. *Lyme Disease*. Mosby Year Book; 1993:49-58.
62. Walsh CA, Mayer EW, Baxi L V. Lyme disease in pregnancy: Case report and review of the literature. *Obstet Gynecol Surv*. 2007;62(1):41-50. doi:10.1097/01.ogx.0000251024.43400.9a
63. Theiler RN, Rasmussen SA, Treadwell TA, Jamieson DJ. Emerging and zoonotic infections in women. *Infect Dis Clin North Am*. 2008;22(4):755-772. doi:10.1016/J.IDC.2008.05.007

64. Qasba N, Shamshirsaz AA, Feder HM, Campbell WA, Egan JF, Shamshirsaz AA. A case report of human granulocytic anaplasmosis (Ehrlichiosis) in pregnancy and a literature review of tick-borne diseases in the United States during pregnancy. *Obstet Gynecol Surv.* 2011;66(12):788-796. doi:10.1097/OGX.0b013e31823e0d0e
65. O’Kelly B, Lambert JS. Vector-borne diseases in pregnancy. *Ther Adv Infect Dis.* 2020;7. doi:10.1177/2049936120941725
66. Dotters-Katz SK, Kuller J, Heine RP. Arthropod-borne bacterial diseases in pregnancy. *Obstet Gynecol Surv.* 2013;68(9):635-649. doi:10.1097/OGX.0B013E3182A5ED46
67. Lambert JS. An Overview of Tickborne Infections in Pregnancy and Outcomes in the Newborn: The Need for Prospective Studies. *Front Med (Lausanne).* 2020;7. doi:10.3389/fmed.2020.00072
68. Souza IE, Bale JF. The diagnosis of congenital infections: contemporary strategies. *J Child Neurol.* 1995;10(4):271-282. doi:10.1177/088307389501000403
69. Bale JF, Murph JR. Congenital infections and the nervous system. *Pediatr Clin North Am.* 1992;39(4):669-690. doi:10.1016/S0031-3955(16)38370-5
70. Huygens A, Marchant A. Fetal infections. *Fetal Therapy: Scientific Basis and Critical Appraisal of Clinical Benefits.* Published online January 1, 2012:200-207. doi:10.1017/CBO9780511997778.024
71. Dennis DT, Hayes EB. Epidemiology of Lyme borreliosis. In: Gray J, Kahl O, Lane RS, Stanek G, eds. *Lyme Borreliosis: Biology, Epidemiology and Control.* CABI Publishing; 2001:251-280.
72. De Koning J, Duray PH. Histopathology of Human Lyme borreliosis. In: Weber K, Burgdorfer W, eds. *Aspects of Lyme Borreliosis.* Springer-Verlag ; 1993:70-92.
73. Duray PH, Steere AC. Clinical pathologic correlations of Lyme disease by stage. *Ann N Y Acad Sci.* 1988;539(1):65-79. doi:10.1111/J.1749-6632.1988.TB31839.X
74. Silver RM, Varner MW, Reddy U, et al. Work-up of stillbirth: a review of the evidence. *Am J Obstet Gynecol.* 2007;196(5):433-444. doi:10.1016/J.AJOG.2006.11.041
75. Goldenburg RL, McClure EM, Saleem S, Reddy UM. Infection-related stillbirths. *Lancet.* 2010;375(9724):1482-1490. doi:10.1016/S0140-6736(09)61712-8
76. McClure EM, Dudley DJ, Reddy UM, Goldenberg RL. Infectious Causes of Stillbirth: A Clinical Perspective. *Clin Obstet Gynecol.* 2010;53(3):635. doi:10.1097/GRF.0B013E3181EB6620
77. Ostrov BE, Athreya BH. Lyme disease. Difficulties in diagnosis and management. *Pediatr Clin North Am.* 1991;38(3):535-553. doi:10.1016/S0031-3955(16)38116-0
78. Eichenfield AH, Athreya BH. Lyme disease: Of ticks and titers. *J Pediatr.* 1989;114(2):328-333. doi:10.1016/S0022-3476(89)80808-X
79. Rahn DW, Malawista SE. Lyme disease: recommendations for diagnosis and treatment. *Ann Intern Med.* 1991;114(6):472-481. doi:10.7326/0003-4819-114-6-472
80. Nadleman R, Wormser G. A Clinical Approach to Lyme Disease. *Mt Sinai J Med.* 1990;57(3):144-156.
81. Agus B. The Recognition and Treatment of Lyme Disease. *Prim Care Update Ob/Gyn.* 1995;2(6):200-203.
82. Trock DH, Craft JE, Rahn DW. *Clinical Manifestation s of Lyme Disease in the United States.*
83. Belani K, Regelman W. Lyme disease in children. *Rheum Dis Clin North Am .* 1989;15(4):679-690.
84. Kullberg BJ, Vrijmoeth HD, Van De Schoor F, Hovius JW. Lyme borreliosis: diagnosis and management. *BMJ.* 2020;369. doi:10.1136/BMJ.M1041