# GESTATIONAL LYME AND ASSOCIATED TICK-BORNE DISEASES

## Introduction:

Ticks carrying Lyme are present in all areas of the US and most countries. Lyme is the most rapidly growing vector-borne illness in the US, according to the CDC, with over 500,000 cases reported annually. It is poorly understood in general, and not often considered in the context of pregnancy. This is a tragic error, as failure to diagnose and treat in pregnancy can result in life-long, severe consequences to the mother and her infant. Fetal consequences include miscarriage, premature labor, cardiac and renal pathology, hydrocephalus, cortical blindness, IUGR, neonatal respiratory distress, fetal death, and SIDS. (1)

## History:

A thorough history will usually reveal exposure risk: gardening, camping, walking in wooded or grassy areas followed by flu-like symptoms, then migratory myalgias, arthralgias, occipital headaches, severe insomnia, fatigue, and memory loss. These episodes may have been recurrent, intermittent, or persistent. A high index of suspicion is critical. It is helpful to ask if the patient has had an unusual response to any antibiotic: myalgias, fatigue, fever, chills, rigors, nausea, vomiting, headache, which may indicate a Herxheimer reaction caused by toxins released by killing Lyme spirochetes.

History of a classic bullseye rash is helpful but present in only about 30% of cases. The symptoms of Lyme disease may have been present but undiagnosed, misdiagnosed, or inadequately treated for years prior to conception, only to diminish or disappear because of the anti-inflammatory effects of pregnancy. Lack of typical symptoms or their severity does not correlate with being disease free. The patient may have had a previous pregnancy while infected with Lyme, and had symptoms abate during the pregnancy. Typically, very soon after delivery, the patient will have had the sudden onset of myalgias, arthralgias, and fatigue, that she may have misinterpreted as postpartum issues. The physician must be aware of this and ask appropriate questions.

Borrelia burgdorferi, the Lyme spirochete, has many forms in the host: motile spirochete, intra-cellular, cystic, persister, and biofilm each requiring a different medication to clear from the host. Borrelia is a uniquely qualified and sophisticated

organism able to enter, live, and persist in humans. Some capabilities, that ensure its survival in a human host, if left untreated, include (2):

1. It can exploit tick saliva proteins to delay early host immune response
2. Deceive alternate complement pathways by masking surface antigens
3. Continuously vary surface antigens to subvert immune response
4. Translocate using uniquely agile motility skills
5. Assume atypical morphologies that subvert both innate and acquired immunity
6. Form persister cells and biofilm colonies which can tolerate antibiotic challenges
7. Able to easily pass through the placenta

Other organisms may have been introduced to the patient with the same tick that harbored Borrelia. These include Bartonella, Babesia, Ehrlichia, Relapsing fever Borrelia, RMSF, and others. This paper will concentrate on the co-infections Bartonella and Babesia. One of the best references for diagnosis and treatment of Lyme and co-infections can be found in Dr. Richard Horowitz's book: How Can I Get Better, available in paperback.

## BARTONELLA

Bartonella is a facultative, intracellular bacteria transmitted by cats and insect vectors: ticks, flees, lice, mosquitoes. It is able to live in epithelial cells of blood vessels and move to invade erythrocytes and can be very persistent, and resist common antibiotics. Symptoms that help to differentiate Bartonella from Lyme include: frontal headaches (Lyme headaches are usually occipital), lymph node enlargement, tender subcutaneous nodules in axilla, on anterior forearms, and lateral thighs, and, especially, bilateral shin pain and pain on bottom of feet in the morning. Striae may be present on back, arms, legs, chest that should not be confused with stretch marks. They are usually horizontal on the back. Bartonella is easily transmitted to the fetus and can cause multiple, chronic problems in both mother and baby.

## BABESIA

Babesia are malaria-like protozoans that invade and reproduce inside RBCs. They have a complex life cycle and may have been present in the same tick that brought Lyme and Bartonella to your patient or may have been transmitted by blood transfusion. It can easily cross to the fetus. Persistent night sweats, chills, and fatigue

are common along with cough and dyspnea. Although rare, Babesia can cause HELLP syndrome, with or without PIH. (3)

## LABORATORY TESTING

The two-tier test, ELISA followed by the western blot if the ELISA is positive, a sequence recommended by the CDC, and IDSA was shown to have at least a 56% false negative rate.(4) The Western Blot (WB) which is more specific, cannot be done unless the ELISA is positive, according to CDC surveillance protocol. The WB can be negative if done less than one month after a tick bite. Interpretation of the WB bands is also flawed. It is not necessary to have two specific IgM or IgG bands to make a diagnosis. One of these will suffice in either IgM or IgG: 18, 23,31,34,39, and 83-93.

The best combination of tests for late or chronic Lyme, includes a CD57 NK white cell total count, which is usually low. LabCorps has a reliable assay. If the patient has had Lyme symptoms less than one year, CD57 is not reliable. IGeneX Lab in California has the most sensitive and specific testing for Lyme. Their Immunoblot test has all Borrelia the antigens found in Europe and North America. Their tests for Bartonella and Babesia are also sensitive and specific. Remember a negative test does not rule out these infections. Your clinical assessment is THE most important consideration.

## TREATMENT PROTOCOLS in PREGNANCY

### LYME DISEASE (Borrelia species)

Lyme disease should be treated through the entire pregnancy whether the infection is acute or chronic. The Lyme Foundation in Hartford, CT maintained a pregnancy registry for ten years in the early 1980's. They found that if adequate antibiotic treatment was maintained, during the ENTIRE pregnancy, that no babies were born with Lyme. That was found to be the case in a review by Charles Ray Jones of 102 children who were born from infected mothers treated with different protocols.(5) CDC and IDSA recommendations for antibiotic dose and duration are suboptimal at best. In general, aggressive oral or parenteral therapy must be used, including bactericidal doses of penicillins, cephalosporins, or erythromycin for the motile form. However, these only kill the spirochete when it is dividing. Unlike other bacteria, it does not need to divide and can change form if threatened. Hence the prolonged treatment and need to continue treatment postpartum.

Because of the expanded blood volume in pregnancy and 50% increase in renal clearance, larger doses of antibiotics need to be used and blood levels need to be done, each trimester, to ensure the MIC is maintained. Probenecid should also be used to

reduce renal clearance of penicillins. I refer you to Dr. Joseph Burrascano's excellent recommendations for treatment in pregnancy (6):

**SAMPLE ANTIBIOTIC PROTOCOLS:**

- Amoxicillin 1 g. Q6h with probenecid 500mg Q8h. Adjust as needed
- Ceftin 1g.Q12h. Adjust as needed
- Benzathine Penicillin 1.2 g. 3 to 4 times per week with probenecid, If oral is not tolerated, then IV meds must be used:
- Ampicillin 1g. Q6h IV
- Ceftriaxone 2g. IV Q12h 4days consecutively each week. Actigall may be used safely for risk of biliary sludging

There are recommendations by Dr. Burrascano for tick bite prophylaxis and Erythema Migrans treatment in pregnancy.

It is essential that the patient take 100 to 200 billion probiotic bacteria daily as soon as the diagnosis is made to avoid having to discontinue treatment because of C. Diff. Herxheimer reactions need to be treated. They will begin to be a problem within one week after starting antibiotics. They cause the body to become acidic. Treatment includes Alka-Seltzer Gold, fresh lemon or lime water three times per day, and sodium bicarb tablets. Supplements to eliminate Lyme toxins include milk thistle, NAC, alpha lipoic acid, and others. Stopping treatment for a short time may be necessary.

## BARTONELLA

Two intracellular antibiotics, rifampin and azithromycin, are recommended to be used concurrently by Dr. Horowitz. Bartonella, like Borrelia, has persister forms and will require several months of treatment.

## BABESIA

Combinations of antibiotics like azithromycin and Mepron are preferable to clindamycin and quinine, which can cause nausea, vomiting, and rashes. Treatment is shorter than the treatment for Lyme and Bartonella. Rarely, Babesia can persist and recur. (7)

## POSTPARTUM

Cord blood and placental tissue should be sampled and sent to the IGeneX lab. Kits are available at IGeneX for samples. After delivery, if the patient has sudden onset of Lyme symptoms, she will need to restart antibiotic therapy immediately. Breastfeeding will have to be worked out with the patient. Lyme has been found in breast milk. Moreover, she will need to treat cystic and biofilm forms until all symptoms have been gone for at least three months. There are several essential oils, stevia, and samento with banderal that may be used to test for a Herxheimer response to ensure that the patient is free of all Lyme forms.

Obviously, these are complex infections and patients should be followed by a high-risk OB specialist and a specialist in treatment of Tick-borne diseases. They can be found at https://www.ilads.org/patient-care/provider-search. Of course, a pediatric specialist should be consulted in advance of labor.

## Erroneous Conclusions from IDSA, CDC, and WHO

1. IDSA 2010 guidelines. They view pregnancy as no different than non-pregnant. “Treatment of pregnant patients for Lyme can be identical to non-pregnant”.
2. CDC 2020, admits that transmission from mother to fetus is “possible but rare”. They will admit that untreated Lyme in pregnancy can lead to infection of the PLACENTA. “Fortunately, with ‘appropriate’ antibiotics there is no increased risk of adverse birth outcomes. There are NO published studies assessing developmental outcomes of children whose mothers had Lyme”.
3. WHO removed stand-alone Congenital Lyme code from ICD-11 codes, in a very non-transparent manner, and stated that there was no need for stand-alone code because there was no recognized “congenital syndrome”.

## RESEARCH GRANTS

It should be noted that congress has heard the Lyme advocacy groups calling for research into better diagnostics and treatment for Tick-borne disease, especially in pregnancy. NIH (NIAID, NICHD) has formally recognized gestational Lyme disease as a research priority to develop new diagnostics, and new technologies to monitor the maternal immune system. DOD has funding for TBD maternal health and adverse outcomes including maternal-fetal transmission. Although welcomed, it will take years for these efforts to bear fruit.

## BIBLIOGRAPHY

1. MacDonald, A. Gestational Lyme Borreliosis. Implications for the Fetus. Rheum Dis Clin North Sm. 1989 Nov.

2. Berndtson, K. Review of evidence for immune evasion and persistent infection in Lyme disease. Int J of Gen Med. 2013
3. Khanguna, R. et al. Babesiosis in Pregnancy: An Imitator of HELLP Syndrome. PMC-NCBI.Jones CR, et al. Gestational Lyme disease case studies of 102 live births. Lyme Times (2005) 34:6.
4. Stricker, R. Let's tackle the testing. BMJ 2007;335
5. Jones, CR. et al. Gestational Lyme disease Case Studies of 102 Live Births, Lyme Times (2005) 34: 6.
6. Burrascano, J. Advanced Topics in Lyme Disease. Sixteenth Edition, October 2008 found online or at ILADS.org
7. Horowitz, R. et al. Maternal Lyme and Babesiosis During Consecutive Pregnancies. A Case Study and Literature Review. ARCH MED CASE REP. 2020; 1-19

**Reviews**

1. Strobino BA, et al. Lyme disease and pregnancy outcome: a prospective study of two thousand patients. Am J Obstet Gynecol. (1993) 169: 367-74.
2. Waddell LA, et al. A systematic review on the impact of gestational Lyme disease on the fetus and newborn. PLoS ONE (2018).
3. Lakos A, et al. Maternal Lyme borreliosis and pregnancy outcome. Int J Infect Dis. (2020)14:e 494-8.

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