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Treatment of Tick Bites and Acute Lyme Disease

A note about testing in early Lyme disease: There is no role for testing for Lyme disease in acute disease. Even Up to Date, a conventional source of online information for physicians, says, “There is no benefit of blood testing for Lyme disease at the time of the tick bite; even people who become infected will not have a positive blood test until approximately two to six weeks after the infection develops (post-tick bite).”¹

Even testing 2-6 weeks after a presumed infection is unreliable. Multiple studies have shown the two-tiered test for Lyme (ELISA followed by a Western blot) to have extremely high false-negative rates.^{2 3 4 5} This is because the test measures our immune response to the bacteria, and *Borellia* is masterful at disguising itself and changing its outer surface proteins to evade detection.⁶

Unattached tick: No action, but if one tick is on you, there is a greater chance that other ticks are as well. Perform careful tick check. Counsel patient to report any symptoms suggestive of tick-borne illness (e.g. rash, fever, headache, malaise, Bell’s palsy).

Attached tick with no rash:

The evidence supports antibiotic prophylaxis rather than watchful waiting to see if an illness develops.⁷ If patient accepts antibiotic treatment, counsel them about possible allergic reactions and recommend use of multi-strain probiotic as well as *Saccharomyces boulardii*. . If patient declines antibiotic treatment, encourage them to report any symptoms suggestive of tick-borne illness (e.g. rash, fever, headache, malaise, Bell’s palsy).

Recommended prophylaxis by ILADS Guidelines.

¹ <http://www.uptodate.com/contents/what-to-do-after-a-tick-bite-to-prevent-lyme-disease-beyond-the-basics>.

Accessed February 3rd, 2016.

² Kaiser R. False negative serology in patients with neuroborreliosis and the value of employing of different borrelial strains in serological assays. *J Med Microbiol* 2000; 49(10): 911-915.

³ Wojciechowska-Koszko et al. Serodiagnosis of Borreliosis: Indirect Immunofluorescence Assay, Enzyme-Linked Immunosorbent Assay and Immunoblotting. *Arch. Immunol. Ther. Exp.* 2011; 59:69-77;

⁴ Ang CW et al. Large differences between test strategies for the detection of anti-Borrelia antibodies are revealed by comparing eight ELISAs and five immunoblots. *Eur J Clin Microbiol Infect Dis.* 2011; 30:1027-1032

⁵ Durovska J et al. Our experience with examination of antibodies against antigens of *Borrelia burgdorferi* in patients with suspected Lyme disease. *Bratisl Lek Listy.* 2010;111(3):153-5.

⁶ Liang FT et. Al. *Borrelia burgdorferi* Changes Its Surface Antigenic Expression in Response to Host Immune Responses *INFECTION AND IMMUNITY* 2004; 72:5759–5767.

⁷ Cameron DJ et al. Evidence Assessments and guideline recommendations in Lyme disease: the clinical management of known tick bites, erythema migrans rashes and persistent disease. *Expert Rev, Anti Infect. Ther.* 2014; 12(9):1103-35

Adult dosing (choose one):

Minocycline 100 mg. twice a day for 21 days.
Cefuroxime 500 mg. twice a day for 21 days.
Amoxicillin 500 mg. twice a day for 21 days.

Pediatric dosing (choose one):

Amoxicillin 50 mg/kg/day in three divided doses, with a maximal daily dose of 1500 mg. for 21 days.
Cefuroxime 20–30 mg/kg/day in two divided doses, with a maximal daily dose of 1000 mg. for 21 days.
Azithromycin 10 mg/kg on day 1 then 5–10 mg/kg daily, with a maximal daily dose of 500 mg. for 10 days.
Doxycycline 4 mg/kg/day in two divided doses, with a maximal daily dose of 200 mg. for either 10 or 21 days. (for children 8 years and older).

Rationale: Transmission rates increase with increasing time of attachment, but there is no definitive cutoff for a safe time. The concept that transmission takes 72 hours may come from the idea that the tick has to regurgitate its stomach contents into the wound. We now know that *Borellia* is present in the tick salivary gland, so transmission may be rapid. A 2015 review article summarizes numerous animal studies showing infection of most animals by 72 hours, and of case reports citing infection within 6 hours or less of humans.⁸ Added to this is the difficulty in knowing how long a very small tick has been attached, as the bite is painless and may go unnoticed. Other tick-borne infections can also be transmitted quickly. *Anaplasma* can be transmitted in a matter of a few hours of tick attachment.⁹ Furthermore, infection can occur even when an EM rash is not present. Estimates of how many patients with documented Lyme disease have a rash ranges from a low of 27% to a high of 80%.¹⁰ In one study, only 20% of cases was the bull's-eye rash present.¹¹

A single 200 mg. dose of doxycycline is inadequate for prevention in many cases. In fact, there is evidence that this may actually decrease the immune response to the infection, causing seronegative infection (where the immune system does not make antibodies, so the patient looks like they do not have the disease).¹² Even a ten-day course has a significant failure rate.¹³ An animal model of infection suggests that the sooner antibiotics are started, the more likely the infection will be prevented.¹⁴ Waiting until a rash develops makes it more likely that the infection will spread beyond the local area and be harder to treat.

⁸ Cook MJ. Lyme borreliosis: a review of data on transmission time after tick attachment. *International Journal of General Medicine* 2015; 8:1-8.

⁹ Thomas RJ, Dumler JS, Carlyon JA. Current management of human granulocytic anaplasmosis, human monocytic ehrlichiosis and *Ehrlichia ewingii* ehrlichiosis. *Expert Rev Anti Infect Ther.* 2009;7(6):709-722.

¹⁰ <https://www.lymedisease.org/lymepolicywork-how-many-of-those-with-lyme-disease-have-the-rash-estimates-range-from-27-80-2>. Accessed February 3rd, 2016.

¹¹ Tibbles CD, Edlow JA. Does this patient have erythema migrans? *JAMA*. 2007; 297(23):2617-27.

¹² Cameron DJ et al. Evidence Assessments and guideline recommendations in Lyme disease: the clinical management of known tick bites, erythema migrans rashes and persistent disease. *Expert Rev, Anti Infect. Ther.* 2014; 12(9):1103-35

¹³ Cameron DJ et al. Evidence Assessments and guideline recommendations in Lyme disease: the clinical management of known tick bites, erythema migrans rashes and persistent disease. *Expert Rev, Anti Infect. Ther.* 2014; 12(9):1103-35

¹⁴ Cook MJ. Lyme borreliosis: a review of data on transmission time after tick attachment. *Int J General Med* 2015; 8:1-8.

EM Rash, with or without known tick bite, WITHOUT systemic symptoms (e.g. fever, joint pain, headache, Bell's palsy):

ILADS Guidelines recommend against any less than 21 days of antibiotics (see rationale above) and prefer 4–6 weeks.¹⁵ Counsel patient in risks of prolonged antibiotic treatment and recommend use of multi-strain probiotic as well as *Saccharomyces boulardii*. Report case of Lyme disease to MN Department of Health.

If the patient still has symptoms at the end of the course of antibiotics, consideration should be given to continuing antibiotics. A different antibiotic may be more effective.

(Choose one):

Amoxicillin 500 mg. 3 times a day or 1000 mg. twice a day for 4–6 weeks

Cefuroxime 500 mg. twice a day for 4–6 weeks

Minocycline 100 mg. twice a day for 4–6 weeks

Azithromycin 250–500 mg. once a day for a minimum of 21 days

Pediatric dosing (choose one):

Amoxicillin 50 mg/kg/day in three divided doses, with a maximal daily dose of 1500 mg. for 4–6 weeks

Cefuroxime 20–30 mg/kg/day in two divided doses, with a maximal daily dose of 1000 mg. for 4–6 weeks

Azithromycin 10 mg/kg on day 1 then 5–10 mg/kg daily, with a maximal daily dose of 500 mg. for 4–6 weeks

Doxycycline 4 mg/kg/day in two divided doses, with a maximal daily dose of 200 mg. (for children 8 years and older) for 4–6 weeks

Rationale: The absence of a known tick bite should not prevent treatment. Only about one third of people with documented Lyme disease recall a tick bite.¹⁶ Especially in areas with high rates of tick carriage of *Borrelia* and *Anaplasma*, the likelihood of infection is high.

Many patients require longer courses of antibiotics, and stopping antibiotics while a patient is still having symptoms increases the risk of relapse.¹⁷ In one study, patients with ill-defined symptoms who had already been treated with antibiotics were found to have positive *Borellia* cultures these patients..¹⁸

EM Rash, with or without known tick bite, WITH systemic symptoms (e.g. fever, joint pain, headache, Bell's palsy):

¹⁵ Cameron DJ et al. Evidence Assessments and guideline recommendations in Lyme disease: the clinical management of known tick bites, erythema migrans rashes and persistent disease. *Expert Rev, Anti Infect Ther.* 2014; 12(9):1103-35

¹⁶ <http://www.uptodate.com/contents/what-to-do-after-a-tick-bite-to-prevent-lyme-disease-beyond-the-basics>. Accessed February 3rd, 2016.

¹⁷ Cameron DJ et al. Evidence Assessments and guideline recommendations in Lyme disease: the clinical management of known tick bites, erythema migrans rashes and persistent disease. *Expert Rev, Anti Infect Ther.* 2014; 12(9):1103-35

¹⁸ Rudenko N et al. Isolation of live *Borrelia burgdorferi* sensu lato spirochaetes from patients with undefined disorders and symptoms not typical for Lyme borreliosis. *Clin Microbiol Infect.* 2015 Dec 8. pii: S1198-743

ILADS Guidelines do not address this specifically. We recommend treating until symptoms have resolved and continuing for an additional 2-4 weeks.¹⁹ Counsel patient in risks of prolonged antibiotic treatment and recommend use of multi-strain probiotic as well as *Saccharomyces boulardii*. Report case of Lyme disease to MN Department of Health. If the patient still has symptoms at the end of the course of antibiotics, consideration should be given to continuing antibiotics. A different antibiotic may be more effective.

Choose one:

Amoxicillin 500 mg. 3 times a day or 1000 mg. twice a day for 4–6 weeks
Cefuroxime 500 mg. twice a day for 4–6 weeks

AND

Minocycline 100 mg. twice a day for 4–6 weeks OR
Azithromycin 250–500 mg. once a day for a minimum of 21 days

Pediatric dosing:

(Choose one):

Amoxicillin 50 mg/kg/day in three divided doses, with a maximal daily dose of 1500 mg. for 4–6 weeks

Cefuroxime 20–30 mg/kg/day in two divided doses, with a maximal daily dose of 1000 mg. for 4–6 weeks

AND

Azithromycin 10 mg/kg on day 1 then 5–10 mg/kg daily, with a maximal daily dose of 500 mg. for 4–6 weeks OR

Doxycycline 4 mg/kg/day in two divided doses, with a maximal daily dose of 200 mg. (for children 8 years and older) for 4–6 weeks

Persistent symptoms after a tick bite or EM rash: The possibility of a persistent infection should be discussed with patients. If the patient responded initially to antibiotics and relapsed after finishing them, there is a significant chance that they have a partially treated infection. An additional 4-6 week course of antibiotics should be considered along with evaluation for co-infections such as Babesia and Bartonella. Referral to a Lyme-literate provider is recommended.

¹⁹ Cameron DJ et al. Evidence Assessments and guideline recommendations in Lyme disease: the clinical management of known tick bites, erythema migrans rashes and persistent disease. *Expert Rev, Anti Infect Ther.* 2014; 12(9):1103-35