



Tick Bite

Kene Isırığı

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Question: What is the risk of Lyme disease after a tick bite? Should we give antibiotic prophylaxis to prevent? **Tanju Meteris, MD**

Cite this article as: Turan C, Hacimustafaoğlu M. Tick bite. J Pediatr Inf 2020;14(2):e87-e89.

Answer (Cansu Turan, MD; Mustafa Hacimustafaoğlu, MD)

Introduction and general information: Before answering these two questions, it will be useful to give some relevant information about the subject. Lyme disease is caused by the genus *Borrelia* (or *Borrelia*) spirochetes and is the most common group of diseases transmitted by the tick in the United States of America (USA) and Europe. *Borrelia burgdorferi* is common in the USA, however, in Europe and Asia, *Borrelia afzelii* and *Borrelia garinii* are more common. The disease is transmitted mainly by the bite of the Ixodes ricinus group ticks infected with *Borrelia*. Lyme disease, initially and the most commonly, involves the skin, and after can disseminate to non-skin disease (involving the joints, nervous system and heart). Ticks can also cause other diseases such as human granulocytic anaplasmosis, babesiosis, ehrlichiosis, rocky mountain fever, tick-borne encephalitis, Crimean-Congo hemorrhagic fever (CCHF). The types of ticks that lead to these diseases may differ from each other. The prevalence of tick types in a region, the frequency of ticks carrying these agents, and the frequency of these diseases may vary in different the geographical locations. Ticks can transmit many other diseases apart from Lyme, including CCHF, anaplasmosis,

ehrlichiosis, which can develop with fever and other findings. In Turkey, *Ixodes* ticks can transmit Lyme disease, and some other ticks (*Hyalomma marginatum* and *Rhipicephalus bursa*) can transmit the CCHF disease. Ticks transmitting Lyme disease are actively present in our country, especially in entire the Black Sea and Marmara regions. Ticks transmitting the CCHF are also seen in Central Anatolia and other regions as well as these regions. In this article, non-Lyme diseases will not be discussed. Tick bites can also cause allergic reactions within the first 24-48 hours at the site where the tick bite, and can also lead to secondary bacterial infections such as staphylococcus and streptococcus after impaired skin integrity.

There are three stages in the life cycles of the ticks: larvae, nymph and adult tick. Lyme disease can be transmitted by nymphs and adult ticks. Since nymphs are smaller, they are harder to see/detect in the body compared to adult ticks.

The risk of developing Lyme disease after a tick bite: Some factors are important in risk assessment for Lyme disease, if detectable after a tick bite. These are; presence of *Ixodes* type ticks (adults are usually hard-shelled, head and neck areas are more prominent), being in the hyperendemic region for this type of ticks, high *B. burgdorferi* infection rate of the ticks,

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Received: 26.06.2020

Accepted: 27.06.2020

Available Online Date: 04.08.2020

swollen appearance of the nymph or adult ticks due to feeding blood, presence of tick more than 36 hours in the skin. After the ticks bite, and after feeding and saturating blood for days, the tick leaves the body itself. Therefore, if the patient has a swollen, enlarged, and round-looking tick, or a similar tick has been seen at home, the risk of disease transmission is likely to be higher.

Ixodes ticks in the nymph stage are typically smaller and rounder (about 1 mm). Adult *Ixodes* ticks are about 3 mm in a blood-free (non-swollen) state and look flatter. However, the size of the ticks that swollen by feeding blood increase to 0.5-1 cm and become more rounded. Blood-fed ticks hold firmly on the skin and are more difficult to remove. A small, round tick that walks on the skin surface or can be easily removed, has possibly not yet begun the feeding process, and therefore does not usually transmit Lyme disease. Feeding ticks release their saliva into the bite site as they absorb blood. However, animal studies have shown that spirochetes are not yet found in tick saliva in the first 48 hours after starting to suck blood. This is important in evaluating a patient with a tick-bite in terms of Lyme disease. Therefore, *B. burgdorferi* is rarely transmitted in the first 36-48 hours of tick adhesion. However, apart from *B. burgdorferi*, which is the cause of Lyme disease, other infection agents such as anaplasmosis, ehrlichiosis, babesiosis which are other zoonoses transmitted by ticks of the genus *Ixodes*; can be transmitted in the first 48 hours of tick bite, since they are found in the infective proportions of the tick salivary glands before the onset of blood feeding.

The tick needs to be infected with *Borrelia* spirochetes in order to infect Lyme disease to humans. In the USA, in the endemic regions in terms of Lyme disease, the rate of infection with *B. burgdorferi* in *I. scapularis*-type ticks was 20-30% in nymphs and 30-50% in adult ticks. Even in high endemic regions, after the bite of the *I. scapularis* tick (deer tick), developing of Lyme disease rate is about 1-3%. In the USA, the annual incidence of Lyme disease in high endemic regions is reported as approximately 0.5 cases/1000 people. In our country, information about the tick types, *Borrelia* infection rate of ticks, Lyme disease development rates in humans after tick bite, and endemicity according to regions are clearly not been established.

In one study, in an endemic region Lyme disease developed in 3.7% (4 cases) of 105 people (109 bites) bitten by ticks. It was observed that the risk increased if the tick remained in the body for a long time. The risk of developing Lyme disease was 1.1% (1/94) in individuals with a tick retention time of < 72 hours, whereas it was 20% (3/15) in those with > 72 hours ($p=0.008$). In this study, *B. burgdorferi* infection (DNA PCR positivity) was found in 14% of ticks.

In a patient presenting with a tick bite, the first job is to remove the tick carefully, and disinfect this area properly. When removing the tick, it should be removed without crushing it, without stressing it (not applying alcohol, olive oil, etc. on the

tick). After removal, the skin should be disinfected, and the hands washed with soap and water. If the parts of the tick, such as the mouth, hose, and neck, remained on the skin after removing the tick, efforts should not be made to re-remove them completely. These remained small parts will spontaneously be excreted by the body later. Afterwards, follow-up of the patient is recommended in the first 48 hours in terms of local allergic reactions and subsequently for the signs of infection due to other agents. In terms of Lyme, it would be appropriate to follow up for a month in terms of erythema migrans, which is the finding of early localized disease in the tick-bite area, and to start treatment if the disease develops.

Antimicrobial prophylaxis after a tick bite: Erythema migrans, a typical clinical manifestation of Lyme disease (early localized disease), occurs in approximately 80% of patients infected with *B. burgdorferi*. Recognition and treatment of the disease at this early stage provides cure in almost all of the cases and prevents the development of early disseminate and late disease. The effectiveness of giving prophylactic antibiotics after a tick bite to prevent Lyme disease has been investigated in different studies. In three separate randomized, placebo-controlled studies, prophylactic amoxicillin given after a tick bite did not protect against the development of Lyme disease later. In the USA, the effect of a single dose of 200 mg oral doxycycline in a hyper endemic region (Lyme incidence 0.05-0.1%) for *I. scapularis* ticks and Lyme disease has been investigated. In this randomized, placebo-controlled, double-blind study, a single dose of 200 mg oral doxycycline was given in 482 adolescents and adult patients, and cases were followed for 6 weeks. In this study, Lyme disease developed in 0.4% (1/235) patients in the doxycycline prophylaxis group, and 3.2% (8/247) in the placebo group ($p<0.04$). In this study, the efficacy of doxycycline was found to be 87% (95% CI; 25-98), and it was calculated that an average of 40 people would need to give prophylaxis to prevent a Lyme case. However, doxycycline caused more side effects (such as nausea, vomiting) than placebo (30.1% vs. 11.1%). In this study, the risk of Lyme disease was 0% (0/59) when the tick looked flat (with no blood-fed), and 9.9% (8/81) in the presence of a blood-fed and swollen tick ($p=0.02$).

In the light of these findings, it is not appropriate to recommend prophylaxis in every tick bite. It would be appropriate to evaluate the patient individually and recommend prophylaxis in the presence of high risk factors. A single dose of doxycycline is recommended prophylactically for preventing Lyme disease in the presence of all of the following risk factors. These risk factors are: in the relevant region, the rate of infection of ticks with *B. burgdorferi* is high (≥ 20), the tick is a blood-fed and swollen appearance, presence of adult or nymphal *I. scapularis* tick (deer tick), the tick has been in the body for at least > 36 hours, prophylaxis can be initiated no later than 72 hours after removal of the tick and no contraindications for doxycycline.

Prophylaxis dose in children is given as 4.4 mg/kg/dose, single dose with maximum 200 mg/dose, orally

Before giving prophylaxis, the patient should be evaluated for the advantages and disadvantages of prophylaxis. The disadvantages of prophylaxis can be summarized as follows: In patients infected with *B. burgdorferi*, the disease can be fully treated and the transition to advanced late stages is prevented by giving antibiotics (doxycycline, amoxicillin, cefuroxime), and complete cure is achieved with the diagnosis of early localized disease in the presence of erythema migrans that develop within weeks after bite. The diagnosis and treatment of erythema migrans is easy. Thus, in many countries and regions where the disease is not frequent, unnecessary use of doxycycline will be prevented. As far as is known, no study is available on this subject, a single dose of doxycycline may alter the nature of the disease and then suppress the clinical diagnosis of Lyme disease. The ability to develop resistance to doxycycline may also be a disadvantage. Repetitive prophylaxis is applied to people who come with frequent tick bites in endemic tick regions where different tick types are frequently found; it may create some other problems such as economic, allergic and developing other resistant microbes. In addition, it may not be rational to give prophylaxis to each tick bite where if there are many types of ticks, and if the *Borrelia* infection rates of these ticks (*B. burgdorferi*, *B. gardinii*, *B. afzelii*) are unknown.

As a result; the risk of Lyme disease is expected to be higher in areas where the tick population that transmits Lyme disease (such as *I. scapularis*) is high, and the ticks are more likely to become infected with *Borrelia*, especially in cases where the tick fed or swollen with blood, the tick remained > 72 hours in the body. In our country, *Ixodes* group ticks can be seen throughout Marmara and the entire Black Sea region, but their infection rate with *Borrelia* is not known. In addition, *B. afzelii* and *B. gardinii* infections are more common in the European region than *B. burgdorferi*. Such *Borrelia* species are less likely to cause extra-dermal disease (joint, facial paralysis, central nervous system and heart) findings, because they are less invasive than *B. burgdorferi*, which is more likely to be disseminated. The early localized of Lyme disease diagnosis (erythema migrans), which is only in the form of skin disease, is relatively easy to diagnose and the therapy is inexpensive and effective.

In conclusion, the answers our friend's question are:

a. Although we do not have detailed data for the risk of Lyme disease after a tick bite in our country, our country does not appear to be hyper-endemic in terms of tick related Lyme disease. In this context, the likelihood of developing Lyme disease after a tick bite can be considered low (possibly 1% and below).

b. In this context, it is not rational to give prophylactic doxycycline to each tick bite event to prevent Lyme disease. It is recommended that doxycycline prophylaxis can be given in the presence of all of the above-mentioned risk factors. In

each case, the tick should be removed properly, and wound care should be performed. In addition, the patient should be monitored closely for the development of erythema migrans (early localized disease) during the first month of tick bite, and appropriate treatment should be given if it develops.

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