

THE MANY FACES OF LYME DISEASE

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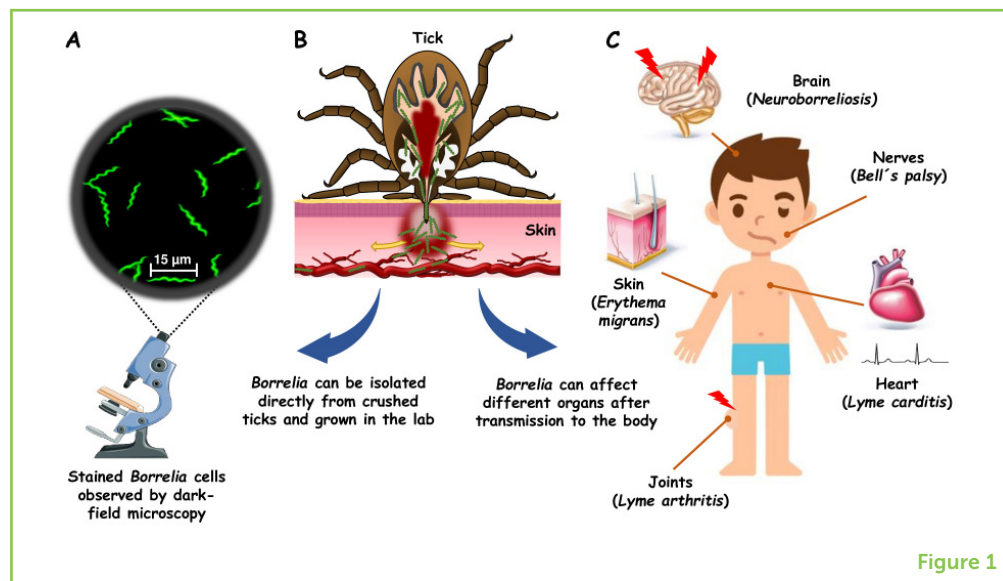
In 1975, many children and adults in Lyme, a coastal town in Connecticut, USA, and the surrounding areas were suffering from severe joint pain. The doctors did not know what caused this mysterious disease, but they knew that the affected children had one thing in common: they had been bitten by ticks! Several years later, scientists discovered that these ticks carried tiny bacteria inside of them. The bacteria were named *Borrelia burgdorferi*, and they were the reason why those children and adults fell ill. *Borrelia* are very small and have a long, corkscrew shape. They can only be observed under a special microscope. Moreover, they can do harm to many different parts of the body. How can such tiny microbes damage the human body, and what can we do to protect ourselves against them? Keep reading to learn more!

INTRODUCTION

The discovery of the bacterium that cause Lyme disease began in the 1970s. Many children in Lyme, a coastal town in Connecticut, USA,

Figure 1

(A) *Borrelia* isolated from ticks can be observed using a dark-field microscope. These tiny bacteria have a typical spiral shape. (B) When a tick feeds on human blood, spirochetes from the tick's gut can move through the tick's mouthparts into the human skin. (C) *Borrelia* can affect various organs and tissues in the human body (Figure of the tick adapted from [1]).

**Figure 1**

and the surrounding areas were suffering from severe joint pain. At first, the doctors did not know what caused this mysterious disease, but they knew that the affected children and also adults had one thing in common: they had been bitten by ticks! Several years later, scientists discovered a bacterium with a typical shape inside the ticks when they used a special microscope. What they observed were very tiny and elongated bacteria which looked like a corkscrew. Later on, the bacteria were named *Borrelia burgdorferi* after the scientist, Willy Burgdorfer, who described these spirochetes in 1981. These tiny bacteria were the reason why those children and adults fell ill. Moreover, they can do harm to many different parts of the body (Figure 1). Keep reading to learn more about ticks, *Borrelia* and the mysterious disease caused by these bacteria!

TICKS—A COZY ENVIRONMENT FOR BORRELIA

Borrelia are often found in the blood of a variety of rodents and birds, so-called **reservoir hosts**. When larval ticks feed on these infected animals, they also consume *Borrelia*, which then reside inside the ticks' guts. When ticks feed on humans, their mouth parts act like a channel or straw, which allows them to ingest blood. As the ticks feed, bacteria can migrate through this channel from ticks to humans (Figure 1) [2]. Several species of ticks have been found to carry *Borrelia*, including blacklegged ticks (*Ixodes scapularis*), western blacklegged ticks (*Ixodes pacificus*), castor bean ticks (*Ixodes ricinus*), and taiga ticks (*Ixodes persulcatus*) [3].

BORRELIA—THE CAUSE OF LYME DISEASE

Borrelia are the causative agents of Lyme disease, but what do they look like? Since *Borrelia* are very small bacteria, we need a special,

RESERVOIR HOSTS

Infected animals (rodents, birds) that often shows no symptoms but can pass bacteria to another organism (ticks), which can then pass it to humans or other animals.

Table 1

Distribution of *Borrelia* species causing Lyme disease and their ticks.

<i>Borrelia</i> species	North America	Europe	Asia	Ticks
<i>B. burgdorferi</i>	Yes	Yes	No	<i>I. pacificus</i> <i>I. scapularis</i> <i>I. ricinus</i>
<i>B. mayonii</i>	Yes	No	No	<i>I. scapularis</i>
<i>B. garinii</i>	No	Yes	Yes	<i>I. ricinus</i> <i>I. persulcatus</i>
<i>B. afzelii</i>	No	Yes	Yes	<i>I. ricinus</i> <i>I. persulcatus</i>
<i>B. bavariensis</i>	No	Yes	Yes	<i>I. ricinus</i> <i>I. persulcatus</i>
<i>B. spielmanii</i>	No	Yes	No	<i>I. ricinus</i>

Table 1

Figure 2

(A) As ticks mature, they go through various stages: larvae, nymphs, and adults. The larvae are often much smaller than the adults, and males are often smaller than females. (B) The various species of ticks that transmit Lyme disease can be found in several areas of the world.

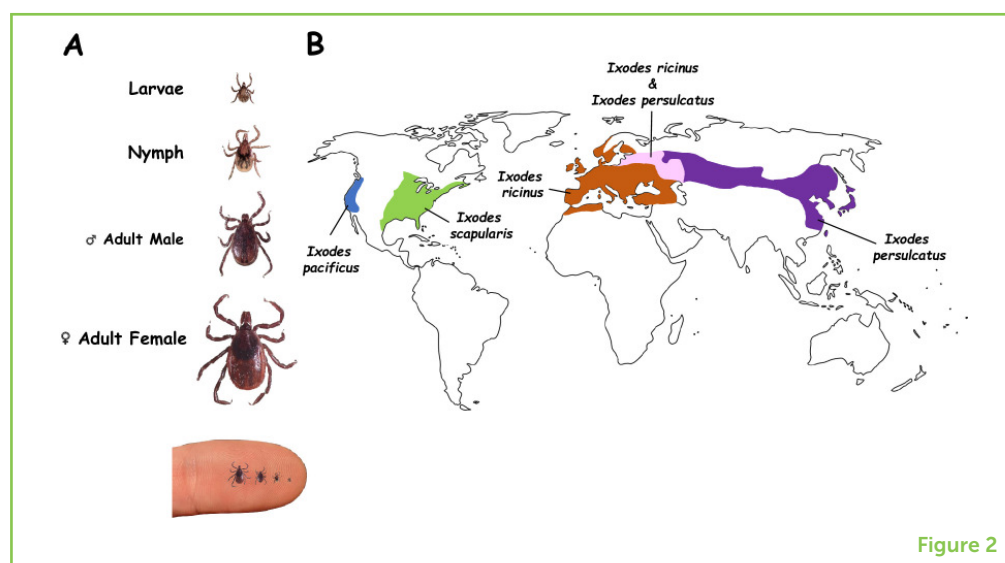


Figure 2

dark-field microscope to observe them. This type of microscope is commonly used to more easily see live biological samples, which absorb little or no light. The unstained bacteria, which have not been prepared with dyes, appear brightly against a dark background. Their shapes can be described best as wavy or corkscrew, and they move around by rotating their bodies (Figure 1).

Borrelia take quite a long time to grow in the lab compared to other bacteria because they divide very slowly. It also can be challenging to grow them because *Borrelia* need a culture medium (bacteria food) that is enriched with proteins, amino acids, salts, and serum collected from rabbits. In comparison to other bacteria, *Borrelia* like to grow at a lower temperature of 33°C and they tolerate only low levels of oxygen. There are at least six different *Borrelia* species found across North America, Europe, and Asia, all of which can cause Lyme disease (Table 1, Figure 2).

IMMUNE SYSTEM

An important network composed of organs and cells which is dedicated to defend and eliminate disease-causing organisms, such as bacteria, viruses, fungi, or parasites. The immune system also recognizes self from foreign cells, and allows survival of harmless bacteria.

¹ For more information on the symptoms of Lyme disease, please visit https://www.cdc.gov/lyme/signs_symptoms/rashes.html.

ARTHRITIS

Joint pain caused by swelling, which can come from a bacterial infection.

NEUROBORRELIOSIS

Symptoms of the nervous system caused by Lyme disease, which can include the inability to control muscle movement in various parts of the body.

ENCEPHALITIS

Inflammation of the brain. The most common symptoms are headache, fever, confusion, neck stiffness, and vomiting.

MENINGITIS

Inflammation of the protective membranes covering the brain and spinal cord. The most common symptoms are fever, headache, and neck stiffness.

WHAT DOES LYME DISEASE FEEL AND LOOK LIKE?

What happens when we are infected with *Borrelia*? We have a great weapon to defend ourselves from dangerous invaders like *Borrelia*: the **immune system**! The immune system consists of cells that flow through the blood like police on patrol, checking for dangerous invaders. As soon as the immune cells detect an enemy, they start pouring out substances that gather more immune cells to help. Other substances directly attack the invaders, to keep the body from becoming ill. However, *Borrelia* manage to survive in the blood despite the immune system's defenses. In fact, *Borrelia* have developed some amazing tricks to overcome the immune system. For example, *Borrelia* can modify some of the structures on their surface, to evade notice. These bacteria can also camouflage themselves by grabbing human proteins from body fluids. Further, *Borrelia* can hide from the human immune response by spending time in body tissues where antibiotics and the immune system hardly penetrate, such as the joint fluid.

Currently, an estimated, 85,000–155,000 people in Europe and ~476,000 people in the USA suffer from Lyme disease every year [4, 5]. The symptoms that may appear after *Borrelia* invade the body typically affect the skin, joints, brain, and heart. After a tick bite, it can take up to 1 month for symptoms to occur. The first symptom of a *Borrelia* infection is often a bull's eye-shaped rash on the skin at the bite site, or swollen earlobes¹. Infected people may also develop fever and headache. You might be familiar with these symptoms if you have ever had a bacterial or viral infection. You probably remember feeling ill and lying in bed most of the day. Lyme disease can cause joint inflammation, called Lyme **arthritis** [6]. This means that literally every little step can hurt, and it might even be too painful to play with other kids. Remember the children in Lyme in 1975? This is what happened to them and why people started searching for the cause of this complex disease.

Children and young people with Lyme disease living in Europe and Asia can develop an infection of the nervous system, which is called **neuroborreliosis**. Milder symptoms of neuroborreliosis can include loss of feeling on one side of the face or inability to move the muscles on one or both sides of the face. This likely happens because *Borrelia* irritate the facial nerve, which is responsible for sensations in the skin of the face and for making facial expressions. Doctors have named this group of symptoms Bell's palsy. *Borrelia* can also cause more severe neurological symptoms, like **encephalitis** and **meningitis**, which is an inflammation of the brain and the spinal cord. Neurological symptoms are serious and require immediate, intensive hospital care. In addition, *Borrelia* can affect the heart, causing shortness of breath or even an irregular heartbeat, which is called Lyme **carditis**.

CARDITIS

Inflammation of the heart which can affect the heart muscle, the normal movement of electrical signals, and the beating of the heart. Symptoms can include shortness of breath or chest pain.

ANTIBIOTICS

Medications of antibacterial substances, which are used to treat and prevent bacterial infections. These compounds kill the bacteria, slow down their growth or prevent spreading through the human body.

HOW CAN YOU PROTECT YOURSELF FROM BECOMING ILL?

The best way to protect yourself from Lyme disease is to protect yourself from ticks. Ticks are most active during the spring and summer seasons, primarily from April to September, but in some areas of the United States, ticks can also start seeking food as early as March. When hiking or playing outside by tall grass, shrubs, or forests during the warm months, make sure to cover as much of your body as possible with clothing. You can also use special insect repellents.

As soon as you get home, check your clothes and every part of your body thoroughly for ticks, in front of a mirror. Ticks love warm areas like the head, neck, armpits, and the backs of the knees. You should also check your bag or anything else you brought with you, including your dog if you took it for a walk. If you discover a tick biting you, it is important to remove it as soon as possible with a special tick removal gadget or tweezers. Never use any other method, like burning it off, crushing it, or using glue to remove it. You should always ask an adult to help you, as it is important to remove the whole tick and not leave any parts in the skin! You might even note the tick bite on your calendar, to make sure you remember it later.

WHAT CAN WE DO TO TREAT LYME DISEASE?

Although all of this sounds scary, there is some good news. Not all ticks carry *Borrelia*, and even if you are bitten by a *Borrelia*-carrying tick, it does not mean you will necessarily become ill from the bite. Fortunately, people who develop symptoms of Lyme disease, like rash or fever, can be treated with various kinds of **antibiotics**. Antibiotics are medicines that travel through the blood to destroy bacteria. To make sure to get rid of all the bad bacteria and to fully recover, it is necessary to take the antibiotics for several weeks [7].

SUMMARY

Now you have learned that ticks can transmit harmful bacteria like *Borrelia* by feeding on blood, and that they can use clever tricks to hide from the human immune system. You have also learned that *Borrelia* can damage our bodies in many ways, so it is important to visit a doctor immediately if you develop any symptoms after a tick bite. It is very important to protect yourself from ticks. If you discover a tick bite, immediately tell an adult. Make sure to properly remove the tick as soon as possible. During the next weeks, pay attention! If you develop any symptoms like a rash, fever, or a headache, or if you generally do not feel well, do not hesitate to see a doctor. Lyme disease can be treated with antibiotics, so a quick diagnosis and treatment will help

to prevent the development of the more severe symptoms of Lyme disease and help you to recover quickly.

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REFERENCES

1. Lin, Y.-P., Frye, A. M., Nowak, T. A., and Kraiczy, P. 2020. New insights into CRASP-mediated complement evasion in the Lyme disease enzootic cycle. *Front. Cell Infect. Microbiol.* 10:1. doi: 10.3389/fcimb.2020.00001
2. Ferrolho, J., Couto, J., Seron Sanches, G., Antunes, S., and Domingos, A. 2018. The secret life inside ticks. *Front. Young Minds.* 6:35. doi: 10.3389/frym.2018.00035
3. Cabezas-Cruz, A., Estrada-Peña, A., Valdés, J., and de la Fuente, J. 2016. Be aware of ticks when strolling through the park. *Front. Young Minds.* 4:24. doi: 10.3389/frym.2016.00024
4. Müller, I., Freitag, M. H., Poggensee, G., Scharnetzky, E., Straube, E., Schoerner, C. H., et al. 2011. Evaluating frequency, diagnostic quality, and cost of *Lyme borreliosis* testing in Germany: a retrospective model analysis. *Clin. Dev. Immunol.* 2012:595427. doi: 10.1155/2012/595427.
5. CDC. 2021. *Lyme Disease. Data and Surveillance.* Available online at: <https://www.cdc.gov/lyme/datasurveillance/index.html> (accessed May 19, 2021).
6. CDC. 2021. *Lyme Disease. Signs and Symptoms.* Available online at: https://www.cdc.gov/lyme/signs_symptoms/index.html (accessed February 1, 2021).
7. CDC. 2021. *Lyme Disease. Treatment.* Available online at: <https://www.cdc.gov/lyme/treatment/index.html> (accessed February 1, 2021).

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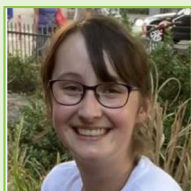
YOUNG REVIEWER



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My name is Ehman and am studing in 7th grade. I enjoy playing basketball and chess, as well as listening to music and playing the bass. My favorite subject is Science and my favorite book is Animal Farm. I want to go into finance when I grow up.

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Yi-Pin is a research scientist in Wadsworth Center, New York State Department of Health at the USA. He is interested in how Lyme disease-causing bacteria spread between ticks and different animals, as well as humans. He also likes to learn from nature, food, and culture in every country (He has been to more than 100 countries from Africa and Asia to Europe, and America, and is exploring the boundary of the world).



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Peter is a professor of medical microbiology, working at Institute of Medical Microbiology and Infection Control in Frankfurt am Main, Germany. His main field of interest is to understand how *Borrelia* hide and overcome human innate immunity. Currently, he supervises several B.Sc., M.Sc., and Ph.D., students who are working in different *Borrelia* projects. During his free time, he likes playing with his grandchildren, gardening, and hiking and walking in the forest or through the beautiful vineyards along the Rhine Valley. *Kraiczky@em.uni-frankfurt.de