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Review Article

Understanding the Tick Borne Disease - Lyme

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Abstract

Infectious diseases are the diseases caused by living organisms (pathogenic microorganisms). They can either be communicable or non-communicable. Communicable diseases are passed from one person to another directly or indirectly (either through body secretions, insects or other means). Many infectious diseases such as measles and chicken pox can be prevented by vaccines. This review article aims to provide a detailed study on Lyme disease. It mainly deals with the disease, symptoms of the disease, its causative agent, diagnosis, prevention, treatment options and current perspectives in its research. Lyme disease is also known as Lyme Borrelia. It is an infectious disease which is spread by ticks. Presently, various kinds of research works are going on regarding this disease, as it plays a havoc, specially in United States and Europe. The consequences of the disease are such that it even gives rise to severe arthritis. Therefore, efforts have to be made how the disease can be effectively treated, if not prevented at all.

Keywords: *Lyme Disease; Tick Borne Disease; World Health Organisation (WHO)*

Introduction

An overview of lyme disease

According to World Health Organisation (WHO), a disease is a particular abnormal condition that negatively affects the structure or function of part, or all of an organism that is not due to any external injury [1]. Zoonotic diseases are infectious diseases of animals which cause diseases when contacted by humans. An example of zoonotic diseases is bird flu. On the basis of the type of causative organism, infectious diseases can be classified as bacterial, viral, fungal, protozoan, parasitic and prion disease. Examples of some common infectious diseases are tuberculosis (caused by the bacteria *Escherichia coli*), common cold (caused by the virus *Herpes simplex*), ringworm (caused by the fungus *Microsporum canis*), malaria (caused by *Plasmodium sp.*). Lyme disease is a bacterial disease caused by *Borrelia bacterium*. Lyme disease is an infectious disease which is spread to humans by the bite of a hard-bodied tick (commonly called deer tick), of the family Ixodidae [2]. Specifically, the tick is *Ixodes scapularis* in the United States and *Ixodes ricinus* in Europe [3], the saliva of which is mainly responsible for the transmission. These ticks have the ability to transmit *Borrelia*, the bacteria which causes the disease in both the tick and humans. Lyme disease is named after a town in Connecticut, where in 1970s some children were affected with arthritis with an unknown cause, known as juvenile rheumatoid arthritis. Later in 1970s, the exact symptoms of the disease were known.

Signs and symptoms of lyme disease

Each patient can develop different symptoms [4]. The symptoms specific to Lyme disease are an expanding area of erythema migrans, which is an expanding area of redness on the skin and bulls - eye rash [5]. Erythema migrans is the first symptom of the disease. Other usual symptoms are fever, headaches, joint pains, neck stiffness, heart palpitations and many others [6].

The symptoms commonly occur in three phases and have diverse effects on different body systems. Neurological disorders can also be a characteristic of this disease [7]. The three phases are:

1. **Early localized infection:** This stage usually does not provide very clear symptoms and so they go unnoticed. The annular rash is the usual symptom, but it is very difficult to notice it in dark skin-tonned people. Some other symptoms like fever and joint pain also persist, but they are usually mistaken to be flu-like symptoms. The body parts most usually invaded by ticks are under-arms, neck, back of knees, where are initial rashes are hard to notice.

2. **Early disseminated infection:** In this stage, the lesions spread to other parts of the body. There is severe neck pain due to swelling of the lymph glands; paralysis of parts or whole of the face, known as Bells palsy may occur; meningitis, heart palpitations and dizziness are also seen in some cases. Another important characteristic of this phase is the untreated patients begin to experience Lyme Arthritis, which is pain and swelling in the large joints.

3. **Late disseminated infection:** Lyme arthritis becomes intense in 60% of untreated patients [8]. Joint pains and other neurological symptoms also worsen.

Diagnosis

Tests to detect Lyme disease are opted mostly when the characteristics of the disease is diagnosed by the presence of symptoms which are confirmed by laboratory tests. In laboratory testing, first a sensitive ELISA is performed; if it yields positive, then a more specific Western blot testing is done [9]. The western blot is done to detect IgA and IgG levels. In some cases, neuroimaging may also be performed, to understand the pathophysiology of the disease, as Neuroborreliosis is a significant manifestation of Lyme disease [10].

Causative agent

Lyme Disease is caused by the bacterium *Borrelia burgdorferi* and *Borrelia mayonii*. They belong to the domain bacteria, phylum spirochaetes, order spirchaetales and family spirochaetaceae. *B. burgdorferi* is named after the scientist, Willy Burgdorfer, who first isolated the bacteria in the year 1982 [11]. Lyme disease is caused by the bite of deer ticks (also called blacklegged tick), which spread *Borrelia* bacteria. The bacteria has a linear chromosome of length 910,725 base pairs. Due to the presence of different linear and circular plasmids, the genome of the *Borrelia* bacteria is said to be unique. A specific plasmid lp25 has been found to be particularly necessary for Lyme disease (*Borrelia Burgdorferi*--MicroWiki). Tick's saliva contains certain biologically active molecules, which facilitate pathogen transmission and infection of the host [7]. The life cycle of ticks and their way of skin tissue injury is shown in the figure 1 and 2 below.

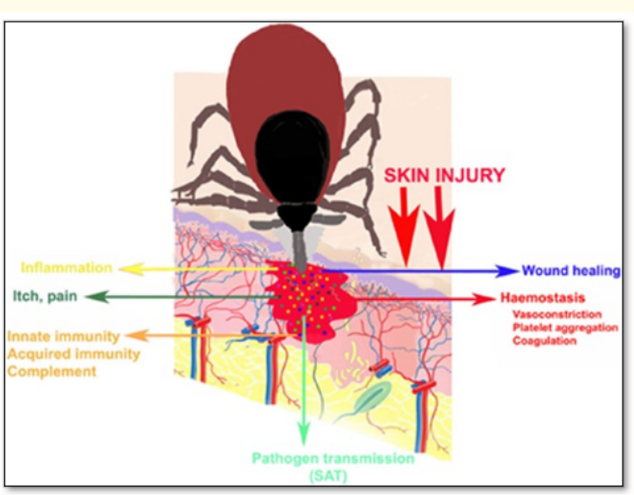

Figure 1: *Skin tissue injury caused by the bite of ticks. Source: Kazimirova., et al. (2013).*

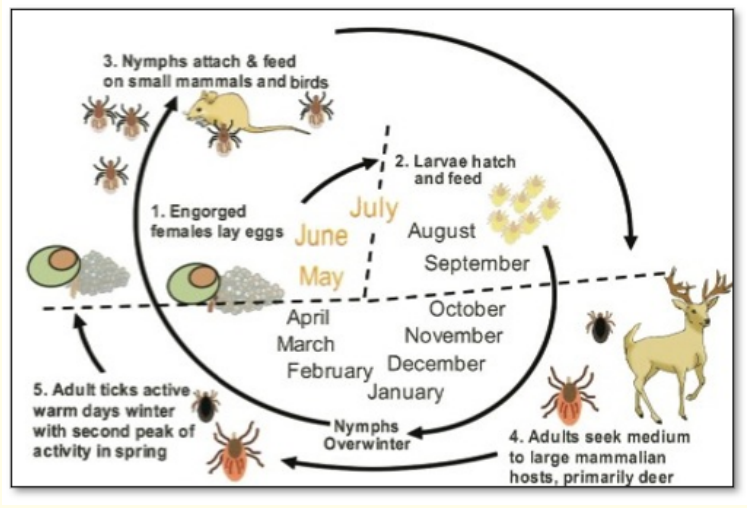

Figure 2: *Life cycle of Ixodes scapularis ticks. Source: https://ehspest.com/ticks.htm.*

Prevention

Most cases of Lyme disease are seen to occur between the months of April to September [12]. Ticks generally prefer moist woodlands having tall trees as their habitats. These are the places where people go for trekking. So, proper protection should be taken while in such trekking camps. In case a tick has sat on the skin surface, it should be immediately removed, using a tweezer if possible. The wound should be properly washed using soap and water. A chemical substance called DEET (N, N-diethyl-m-toluamide) is used as a repellant for ticks.

SmithKline Beecham developed a recombinant vaccine against Lyme disease, based on the outer surface protein A of *Borrelia burgdorferi* [13]. Furthermore, current researches are going on for the development of a new vaccine, which is being engineered to target the OspA protein of *Borrelia burgdorferi*.

Treatment

The primary treatment is done using antibiotics [8]. The antibiotic selection, administration route and the duration of the therapy is decided by the stage of Lyme disease that the concerned patient is in, the clinical symptoms he/she is exhibiting, any other medical complications of the patients and fixed drug reaction or allergy of the patient to certain drugs [14]. The antibiotic doxycycline is administered orally to treat early Lyme disease and other neurological complications. Also, antibiotics such as minocycline, azithromycin, amoxicillin, or cefuroxime axetil antibiotics are administered for treatment of the first two stages of Lyme disease [15]. Rare cases developing Lyme carditis, may require a temporary pacemaker [16]. In the last stage where symptoms worsen, antibiotics such as ceftriaxone or penicillin may be administered. Non-steroidal anti-inflammatory drugs are used to treat the pain due to Lyme arthritis [15].

Doxycycline and minocycline are broad spectrum antibiotics, belonging to the tetracycline family [17]. These drugs inhibit the protein synthesis of the bacteria and are thus bacteriostatic in nature. At the ribosome, which is the site for protein synthesis, these drugs prevent the amino acyl tRNA to bind to the acceptor site of the mRNA-ribosome complex [18]. Such antibiotics also mediate the inflammatory effects brought about by the lipoproteins of the *Borrelia* bacteria. They also treat the inflammations caused by the left over bacterial debris after the death of the bacteria.

It has been seen that although these antibiotics are effective in the treatment of Lyme disease, about 10% of the patients develop a condition called Post Lyme Disease Syndrome (PTLDS).

Current perspectives

The Centres for Disease control and prevention (CDC) has classified Lyme Disease as an emerging infectious disease, which is being spread to various parts of the world, especially United States. A detailed analysis of the genome and pathogenome has been done, which proves to be very beneficial towards better understanding of the disease [19]. Recently, Lyme disease is emerging as a serious public disease in Canada. Several researches and guidelines are being prepared to prevent the disease and develop better treatment options [20]. Also, most of the current researches ongoing are on the mechanisms of entry of the bacteria into the human body, so that more effective treatment procedures can be developed to combat the disease [21].

Conclusion

In conclusion, it can be said that Lyme disease is gradually becoming a widespread bacterial disease. So, steps should be taken to prevent the disease effectively. Children should be regularly administered with the vaccine. In case, the disease still occurs, it should be treated as early as possible and with appropriate medicines. The present researches going on in this area will help combat the disease with better methods gradually. Better vaccines are yet to be developed to immunize the people from the disease. Generally, the sequenced genome of *B. burgdorferi* does not contain any obvious genes coding for pathogenesis. Improper use of antibiotics may develop resistance in the bacteria against the antibiotics and may cause serious impact in the treatment procedure. Thus, the mechanisms of *B. burgdorferi* infections are still an important ongoing research field.

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