e- ISSN 0976-0342
Print ISSN 2229-7456

International Journal of Pharmacy & Therapeutics

Journal homepage: www.ijptjournal.com

Review article

LYME DISEASE AND ITS COMPLICATIONS: A REVIEW

G. Sangeetha Roy[1*], SK. Banu Tahrunnisa[1*], S.Mounika[1], K.Sai Krishna[1], Rajani Gunnam[1]

[1]Department of Pharmacy Practice, KLR Pharmacy College, Paloncha, Kothagudem

ABSTRACT

Lyme disease is a most common vector-borne multisystem disease caused by bacteria *Borreliaburgdorferi*, in the United States, Europe and Asia and is transmitted to humans by the bite of the Ixodes (deer) tick. The disease may occur most frequently during spring, summer, May, mid-October and early November and untreated infection can spread to other parts of the body within days or weeks, causing more serious skin, neurologic, cardiac and joint abnormalities and over months or years, oligo-articular arthritis, peripheral neuropathy, or encephalopathy. The aim of our article primarily reviews disease's complications and summarizes the, pathogenesis, clinical features, epidemiology, diagnosis, treatment and prevention of the chronic disease.

Key Words:-Lyme disease, Borreliaburgdorferi, Ixodes (deer) tick, Complications.

Access this article online		
Home page: http://ijptjournal.com/ DOI: http://dx.doi.org/10.21276/ijpt.2019.10.1.3		Quick Response code
Received:01.11.18	**Revised**:12.11.18	**Accepted**:05.12.18

Corresponding Author

G. Sangeetha Roy

Department of Pharmacy Practice, KLR Pharmacy College, Palvoncha, Bhadradhi Kothagudem - 507115, India.

Email:- bannuaba12@gmail.com

INTRODUCTION

Lyme disease is a multisystem illness (Adrianar. Marques et.al 2010) caused by bacteria *Borreliaburgdorferi*, is the most common vector-borne disease in most of the countries that are transmitted to humans through a bite from an infected black-legged or deer tick(John Aucott*et al*., 2016). Lyme disease was initial described in 1977 following investigation of a cluster of arthritis cases among children living near Lyme, Connecticut (steere AC Malawista SE *et al*., 1977). In 1981, a bacterial spirochete, Borreliaburgdorferi, was identified in Ixodesscapularis (Burgdorfer W *et al*., 1982) and later demonstrated to be the etiologic agent of Lyme disease (Benach JL *et al*., &streere AC *et al*., 1983). B. burgdorferi happens naturally in reservoir hosts, together with mice, squirrels, shrews, and alternative small vertebrates (Dennis DT *et al*., 2005). Ixodesscapularis and I. pacificus (also referred to as black-legged or deer ticks) become infected with B.burgdorferi whereas feeding on the blood of natural reservoir hosts. In humans, infection with B.burgdorferi can result in dermatological, musculoskeletal, neurologic, or cardiac abnormalities (Shaeiroed *et al*., 2000, Steere AC et.al 2004 &Wormser GP *et al*., 2006). The clinical presentation varies depending on the stage of the illness and includes erthymamigrans, carditis, central nervous system disease, and arthritis (Thomas S.Murray *et al*., 2010).

Microbiology and Pathogenesis

The genus Borrelia is a member of the family Spirochaetaceae, which also includes Leptospira and Treponema. Spirochetes have a crinkly body and flagella enclosed between the outer and inner membranes (Adriana R.Marques*et al*., 2010). The organism has been sub-classified into several genomospecies, including B. burgdorferisensustricto, B. garinii, B. afzelii and others (Thomas S.Murray*et al*., 2010).

Lipoproteins play a crucial role within the life cycle of B. burgdorferi and account for a major a part of the B. burgdorferi genome. Lipoproteins have differential expression in culture, within the tick, and in the

mammalian host. for example, outer surface protein an (OspA) and outer surface protein B (OspB) are expressed abundantly in culture. OspA is also expressed within the tick gut, where it mediates true bacteria attachment (Pal U *et al*., 2000). As an infected tick begins to feed on a mammal, the synthesis of OspA is inhibited and that of outer surface protein C (OspC) is induced (Schwan TG *et al*., 1995). OspC is very important within the transmission of the true bacteria from tick to mammal, and it's needed early in class infection (Tilly K *et al*., 2006). OspC is extremely diverse, and OspC alleles are linked to both infectivity and invasiveness. (Lagal V *et al*., 2003 &Seinost G, *et al*., 1999). The spirochete's ability to spread through skin and alternative tissues may be facilitated by the binding of OspC to human plasminogen. (Coleman JL *et al*., 1997). This dissemination from the site of the tick bite, via the bloodstream, produces the systemic systems that may be associated with early Lyme disease as well as the clinical manifestations of early disseminated and, ultimately, of late Lyme disease. In humans with erythema migrans, infiltrates of macrophages and of T cells produce both inflammatory and anti-inflammatory cytokines (Mullegger RR *et al*., 2000). There is also evidence that in disseminated infections, adaptive T-cell and B-cell responses in lymph nodes produce antibodies against many components of the spirochete (Fikrig E *et al*., 1998 & Krause A, *et al*., 1991). During dissemination within humans, B. burgdorferi attaches to certain host integrins (Coburn J Leong JM *et al*., 1993 & Coburn J, *et al*., 1998) eliciting a pro-inflammatory response (Behera AK *et al*., 2008), that includes production of both matrix glycosaminoglycans, and extracellular-matrix proteins (Guo BP *et al*., 1998 &Probert WS *et al*., 1998) which may explain the organism's tropisms for particular tissues (e.g., collagen fibrils in the extracellular matrix in the heart, nervous system, and joints)(Guo BP *et al*., 1998).

Synovial tissue from patients with Lyme arthritis typically shows synovial hypertrophy, vascular proliferation, and a marked mononuclear cell infiltrate. Sometimes pseudolymphoid follicles are present that resemble peripheral lymph nodes (Probert WS *et al*., 1998). During acute Lyme arthritis, innate immune responses to B. burgdorferi lipoprotein, as well as marked adaptive immune responses to many spirochetal proteins, are found (Steere AC et.al., 1988, Akin E *et al*., 1999 & Vincent MS *et al*., 1998).Both Th-1 and Th-2 dependent cytokines are found in the joint fluid (Chen J *et al*., 1999 & Gross DM *et al*., 1998). In addition, patients with Lyme arthritis typically have higher Borrelia-specific antibody titers than do patients with other manifestation of Lyme disease (Steere AC et.al., 1988 & Yin Z et.al., 1997). Some adult patients with lyme arthritis, particularly those with HLA-DRB1 alleles, can develop a chronic, antibiotic treatment resistant, autoimmune arthritis. (Dressler F et.al., 1993, Steere AC et.al., 1994 &Steere AC *et al*., 2006). In just about 70%–80% of cases, patients develop a characteristic rash, erythema migrans (EM), among 30 days of infection with B. burgdorferi.

EM could be a red expanding rash, with or without central clearing, which regularly is accompanied by symptoms of fatigue, fever, headache, mild stiff neck, arthralgia, or myalgia. at intervals days or weeks, untreated infection will spread to alternative parts of the body, inflicting a lot of serious medical specialty conditions (e.g., meningitis, radiculopathy, and facial palsy) or viscus abnormalities (e.g., inflammation with atrioventricular heart block). Over a amount of months or years, untreated infection will lead to mono- or oligoarticular arthritis, peripheral neuropathy, or encephalopathy. (Fig- 1).

Epidemiology

The risk for acquiring lyme disease within the u. s. varies with the distribution, density, incidence and prevalence of infection in ticks. Most cases of lyme disease occur within the north-eastern and north-central states (Bacon RM *et al*., 2008). lyme disease is also endemic in many regions in Europe and Asia. The percentage of the population testing positive for anti-Bb antibodies varies in several European countries (approximately 5-25%). some of these patients don't have any symptoms of lyme disease. Lyme borreliosis is most prevalent in Central and jap Europe. In European country and slovenia it reaches 120-130 cases per 100,000 inhabitants. In poland some seven thousand new cases were reported in 2007 (Derdakova M *et al*., 2005, Asbrink E *et al*., 1993, Hubalek Z *et al*., 1997, Nau R *et al*., 2009 &Stanek G *et al*., 2012). In recent years, over 30,000 cases of lyme disease are reportable annually to the Centers for disease control and prevention (CDC), and in a third of reportable cases, inflammatory disease was a manifestation of the disease (Bacon RM *et al*., 2008). However, the new estimate supports studies published within the 1990s indicating that verity number of cases is between 3- and 12-fold higher than the amount of reportable cases(CDC estimates of Americans diagnosed with Lyme Disease, 2013).

Borreliaburgdorferi is transmitted to humans by arthropod genus ticks. These little, dark-colored ticks have a 2-year life cycle made of four developmental stages: egg, larva, nymph, and adult. Eggs are laid in spring and hatch into larvae throughout the late summer. Larvae feed on little animals (usually mice) and may acquire B. Burgdorferi infection at this stage. The larvae then molt into nymphs, that feed again the following spring to early summer (and might transmit the infection to the new host). Nymphs molt into adult ticks in mid-october and early-November, once the adult female ticks feed again, primarily on large animals. small mammals

are vital within the transmission cycle of B. burgdorferi, as some, notably the white-footed mouse, might stay infected however asymptomatic and so function reservoirs for the organism. Some avian species also might function reservoirs for B. burgdorferi. deer are vital because they're the principal hosts for the adult ticks, though they're not reservoir competent for B. Burgdorferi(Adriana R. Marques *et al*., 2010).

And conjointly usually the life cycle of ticks, that kill blood one time in every of 3 stages (larva, nymph and adult tick). Larvae emerge from eggs laid in spring, attach to little vertebrates, World Health Organization area unit their initial hosts, associated become infected with spirochetes once attached to an infected host. Larvae molt into nymphs, and through the following spring and summer, from mid-may to late July, the nymphs feed for the second time. Tick nymphs before the meal area unit only the dimensions of a poppy seed and so tough to note, however area unit terribly active in transmitting a BB shot infection which may cause various infections in humans. In late summer the nymphs remodel into adult forms (the size of associate apple seed) and in time of year or maybe in winter, adults feed on a 3rd host and reproduce; then the life cycle repeats (Stanczak J *et al*., 1999 & Thomas S.Murray*et al*., 2010).

"The new preliminary estimate confirms that lyme disease could be a tremendous public health problem within the u. s., and clearly highlights the urgent want for prevention." (CDC estimates of Americans diagnosed with Lyme Disease, 2013).

CLINICAL MANIFESTATIONS

Symptoms (Fig- 2)

Early Localized Lyme disease (Stage 1) Symptoms begin from days or weeks after infection. They are similar to the flu infections and may include:

- Fever and chills, swollen lymph nodes, itching sensation and rashes, general ill feeling, headache, joint pain, muscle pain, stiff neck.

There is also a "bull's eye" rash, a flat or slightly raised red spot at the positioning of the tick bite. Often there is a clear area in the centre. It can be large and expanding in size. This rash is called erythema migrans. Without treatment, it can last four weeks or longer. Symptoms may come and go. Untreated, the bacterium can spread to the brain, heart, and joints.

Early Disseminated Lyme arthritis (Stage 2) Symptoms could occur weeks to months once the tick bites, and will include:

- Numbness or pain within the nerve space.
- Paralysis or weakness within the muscles of the face.
- Heart problems, like skipped heartbeats (palpitations), chest pain, or shortness of breath.

Late Disseminated Lyme arthritis (Stage 3) Symptoms will occur months or years once the infection. The foremost common symptoms are muscle and joint pain. Other symptoms could include:

- Abnormal muscle movement, joint swelling, muscle weakness, numbness and tingling, speech issues, thinking (cognitive) issues (Allen C. Steere*et al*., 2016)**.**
- **Complications**
- Untreated Lyme disease can cause the following complications
- **Erythema migrans** is usually asymptomatic but may be painful, and it may be accompanied by systemic findings such as fever, malaise, headache, regional lymphadenopathy, stiff neck, myalgia, or arthralgia.(Fig-3)
- **Cranial nerve palsies,** particularly facial nerve palsy, and meningitis (sometimes accompanied by papilledema and increased intracranial pressure).
- **Lyme arthritis** is usually mono-articular but may also be oligo-articular and primarily affects the large joints, particularly the knee. Lyme arthritis can be difficult to distinguish from septic arthritis.
- **Carditis,** which usually is manifest as a prolonged PR interval or, sometimes, complete heart block, is a rare manifestation of early, disseminated disease. Patients may present with fatigue, dizziness or syncopal episodes.
- **Borreliallymphocytoma,** an inflammatory infiltrate that typically occurs in the ear lobe or the breast, is seen with some frequency in patients with Lyme disease.
- **Meningoradiculoneuritis**(Bannwarth's syndrome), sometimes painful radiculopathy due to Lyme disease.
- **Encephalitis, encephalopathy**, and **polyneuropathy** are also manifestations of late Lyme disease, but they are very rare in children.
- **Acrodematitis chronic atrophicans,** chronic sclerosing dermatitis, is an uncommon manifestation of Lyme disease(Thomas S.Murray*et al*., 2010).
- **Cognitive defects**, such as impaired memory.
- **Death,** Untreated complications may even lead to death

Diagnosis

- Diagnosis of early Lyme borreliosis related to EM wants no serological testing. It must be noted that EM usually appears within 2-30 days after the tick bite, while anti-Bb antibodies appear approximately 2-4 weeks after the initial tick bite. Thus, the patient with EM may have negative serological test results (Flisiak R, Prokopowicz D *et al*., 2000 &Flisiak R, Pancewicz S *et al*., 2008). Serological testing is predicated on detection of antibodies against spirochetal antigens. Two-step diagnosing is necessary: the primary step is predicated on a high sensitivity ELISA check, and positive results ought to later be confirmed by aa lot of specific Western

blot assay. Humoral response starts with immunoglobulin antibodies, which usually appear 2 to 4 weeks after infection. Their levels peak eight to ten weeks when infection then bit by bit disappear, however in some patients might persist for many years. Immunoglobulin G (IgG) antibodies appear in serum 6 weeks after infection, reach their peak levels after 4 to 6 months and are detectable in serum for many years (Wormser GP *et al*., 2000, Gasiorowski J *et al*., 2007 &Hermanowska-Szpakowicz T *et al*., 2000). In patients where CNS borreliosis causes de-myelination, anti-myelin antibodies are detected in the serum and cerebrospinal fluids (CSF). Imaging studies reveal disseminated de-myelination of cerebral white matter, depicted as hypo-dense lesions in a computed tomography (CT) scan and disseminated hyper-intense lesions in magnetic resonance imaging (MRI). The CSF analysis is useful within the identification of Lyme borreliosis in these cases. In meningitis the CSF cell count is increased to several dozen or several hundred cells per millilitre, accompanied by a slightly elevated CSF protein level and specific intrathecalIgG or IgM antibody synthesis, detected using the ELISA test (Hermanowska-Szpakowicz T *et al*., 2000).

Treatment

In most cases, Lyme disease is treated successfully with antimicrobial therapy (Tables 1 and 2). Oral medical care is suggested for early and uncomplicated infection, together with isolated facial nerve palsy. Doxycycline and amoxicillin are the drugs of choice. Doxycycline has the advantage of being effective against human granulocytic anaplasmosis (HGA), but it is contraindicated in children younger than 8 years of age and in pregnant or lactating women. During antibiotic drug therapy, patients ought to be suggested to wear sunscreen and avoid sun exposure, because the drug might cause sensitivity. Amoxicillin is that the drug of alternative for kids younger than eight years getting on and pregnant or breast feeding ladies. Cefuroxime axetil could be a second-line various because of its slighter higher price. Oral macrolides are considered third-line alternatives, as their clinical efficacy has been less than that of the β-lactams and tetracyclines(Adriana R. Marques *et al*., 2010). Treatment of Lyme borreliosis in the phase of Erythema migrans (EM) or borreliallymphocytoma consists of doxycycline, amoxicillin or cefuroxime axetil. Arthritis is treated with oral antibiotic drug, Polymox or cephalosporin axetil, while neuroborreliosis, recurrent arthritis and heart involvement ar treated with Rocephin, Mefoxin or benzylpenicillin. During treatment, non-steroidal anti-inflammatory agents (NSAIDs), such as ibuprofen or naproxen, may be used for pain (Sheila L. Arvikar*et al*., 2015). The ACA is treated with amoxicillin, doxycycline, Rocephin, cefotaxime and penicillin g (GrażynaBiesiada*et al*., 2012).Parenteral antibiotics generally are recommended for treating neurologic Lyme disease and for the initial therapy of patients with more severe cardiac disease (i.e., those with symptoms, second- or third-degree atrioventricular block, or first-degree block with a PR interval ≥0.3 seconds)(Adriana R. Marques *et al*., 2010).

- Sometimes failures occurred rarely with all these regimens. More severe cardiac disease requires hospitalization for cardiac monitoring. In late disease, the response to medical care could also be delayed for many weeks to months.

Prevention

- Patients should be instructed in measures that help avoid ticks, including walking in the centre of a path, avoiding brushy areas, and wearing appropriate clothing (i.e., light-colored clothing, which facilitates spotting of the ticks, long-sleeved shirts, and pants tucked into socks or boot-tops). In endemic areas, cleaning brush and trees, clearing leaf litter and woodpiles, and keeping grass trim may lessen the exposure to ticks. Application of pesticides to residential properties is effective in suppressing populations of ticks however could also be harmful to alternative wildlife and people (Eugene D. Shapiro *et al*., 2014). Other proceedings, such as applying insect repellent, checking for ticks daily, and removing them immediately if found, will help avert infection because transmission of B. burgdorferi from an infected tick induces with time of attachment. Post-exposure antimicrobial prophylaxis for Ixodesscapularis bites with a single 200-mg dose of oral doxycycline may be considered for patients (who have no contraindications to the drug) when 1) the incidence of B. burgdorferi infection is at least 20% in ticks in the patient's area, 2) the tick was sustained for at least 36 hours, and 3) prophylaxis can be initiated within 72 hours after the tick was removed. Serologic testing of Lyme disease patients and testing the ticks for infection with B. burgdorferi are not helpful. All patients should be monitored closely for up to 30 days for signs and symptoms of tick-borne diseases. Vaccine (OspA-based) for preventing Lyme disease in humans was approved by the FDA in 1998 but withdrawn from the market in 2002 because of poor sales and theoretic concerns about triggering autoimmune arthritis.

Summary

At a point, immense evidence shows that prolonged antibiotic therapy, as tested in the other clinical trials, does not offer lasting or substantive benefit in treating patients who have Lyme disease syndrome. Therefore, it is right to go forward to test other approaches that may help such patients. The health care provider taking care of such patients, without fail, one should review carefully to give credence for the diagnosis of Lyme disease and

should think little of these patients can develop other unrelated conditions. It is necessary that patients be offered the best advice based on current, evidence-based information (Burdge DR *et al*., 1993). Most importantly, there should be a collaborative approach to the treatment process with the patient. With anticipation, further research to understand the complications of Lyme disease and the reasons undivulged sustained symptoms after Lyme disease will lead to the development of beneficial therapies(Adriana R. Marques *et al*., 2010).

ACKNOWLEDGEMENT

Nil

CONFLICT OF INTEREST

No interest

Table 1. Antibiotics used for the treatment of Lyme disease

Oral agents		Adult dosage	Pediatric dosage	Comments
Preferred	Doxycycline	100 mg twice/d	Children >8 y old: 4 mg/kg/d divided in 2 doses (maximum 100 mg/dose)	Active against HGA. Contraindicated in pregnancy, lactation, and children younger than 8 y
	Amoxicillin	500 mg every 8 h	50 mg/kg/d divided in 3 doses (maximum 500 mg/dose)	–
	Cefuroxime axetil	500 mg twice/d	30 mg/kg/d divided in 2 doses (maximum 500 mg/dose)	Useful when cellulitis cannot be ruled out. More expensive.
Alternative	Azithromycin Clarithromycin Erythromycin	500 mg/d 500 mg twice/d 500 mg 4 times/d	10 mg/kg/d (maximum 500 mg/d) 7.5 mg/kg twice/d (maximum 500 mg/dose) 12.5 mg/kg 4 times/d (maximum 500 mg/dose)	Patients treated with macrolides should be observed closely because of the risk of failure. In 1 trial, adults with erythema migrans were more likely to fail therapy if treated with azithromycin for 7 d than if treated with amoxicillin
Intravenous agents				
Preferred	Ceftriaxone	2 g/d IV	50–75 mg/kg/d (maximum 2 g/d)	Easy to administer and largest experience in Lyme disease. It can cause biliary complications.
Alternative .	Cefotaxime	2 g IV every 8 h	150–200 mg/kg/d IV divided into 3 or 4 doses (maximum dose 6 g/d)	Efficacy possibly same as that of ceftriaxone but requires more frequent administration
	Penicillin G	18–24 MU/d IV divided every 4 h	200,000–400,000 U/kg/d divided every 4 h (maximum dose 18–24 MU/d)	More frequent administration. May be less effective than Ceftriaxone

Table 2. Lyme disease: recommendations for therapy of complications

Clinical Manifestation	Treatment Regimen	Duration (days)
Erythema migrans (single or multicle)	Oral	14 (14-21)
Isolated facial nerve palsy	Oral	14 (14-21)
Meningitis, radiculoneuritis	Intravenous	14 (10-28)
Mild cardiac disease	Oral	14 (14-21)
More severe cardiac disease	Intravenous (may complete regimen with oral therapy)	14 (14-21)

Late neuroborreliosis	Intravenous	14 (14-28)
Lyme Athritis	Initial therapy with oral regimen. May repeat oral therapy or give IV therapy if response is not satisfactory. Patients who do not respond may have antibiotic-refractory Lyme arthritis.	Oral regimens: 28 IV therapy: 14 (14-28)

Fig1. Morphology and cellular architecture of *Borreliaburgdorferi*

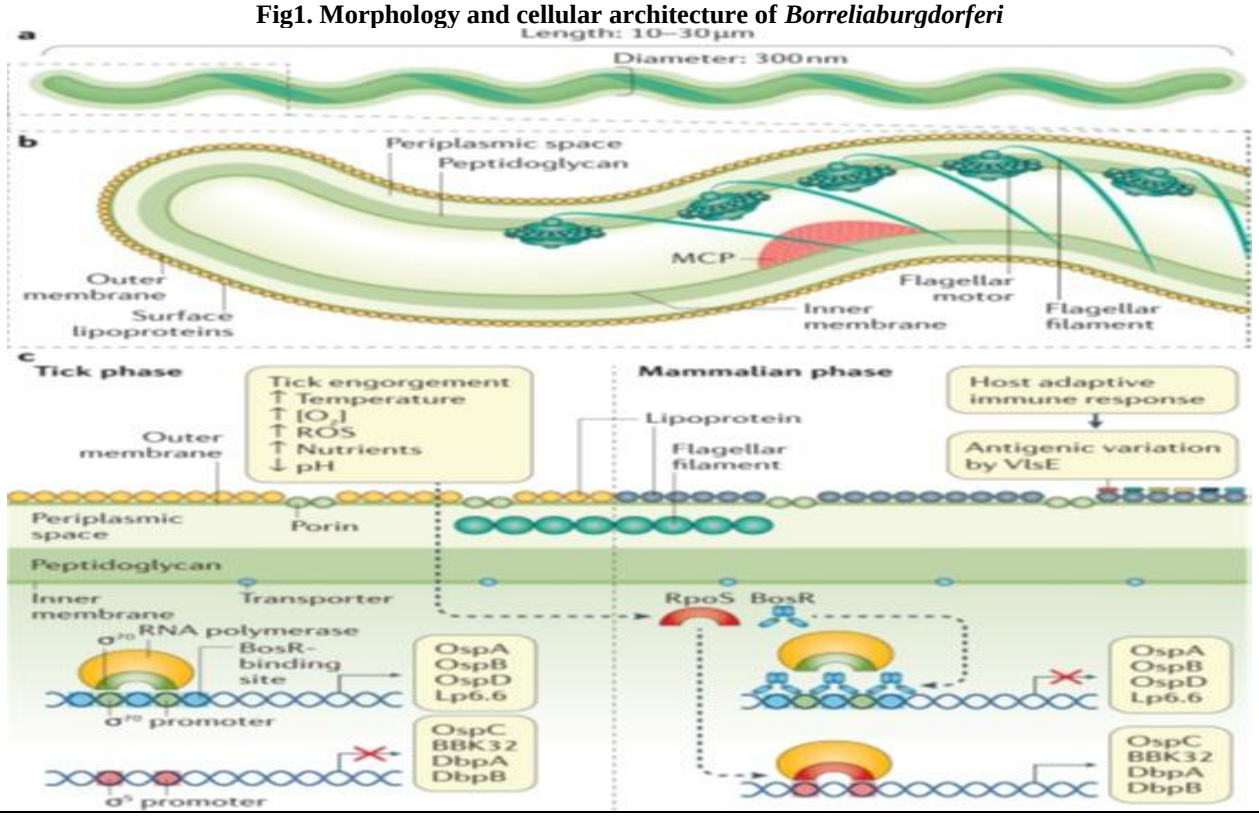


Fig2. Stages and common clinical Manifestations of Lyme borreliosis

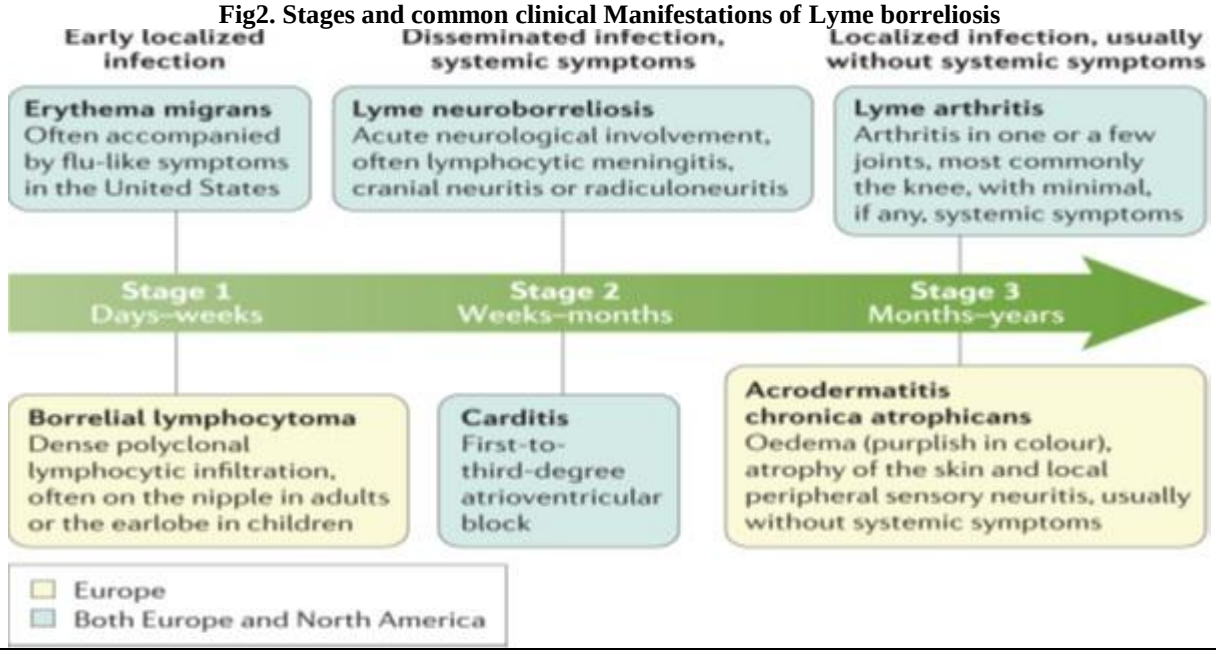
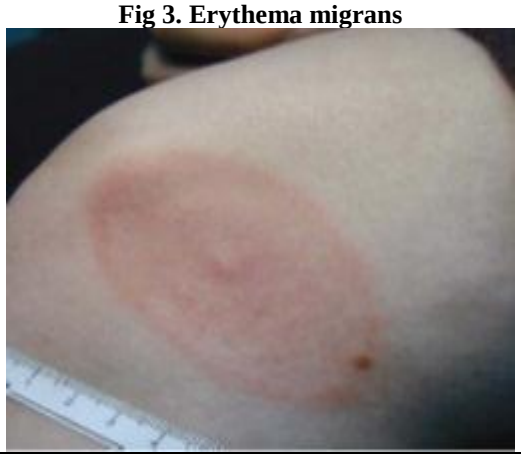


Fig 3. Erythema migrans



REFERENCES

Adriana R. Marques. Lyme Disease: A Review. *Curr Allergy Asthma Rep*, 10, 2010, 13–20.

Akin E, McHugh GL, Flavell RA. The immunoglobulin (IgG) antibody response to OspA and OspB correlates with severe and prolonged Lyme arthritis and the IgG response to P35 correlates with mild and brief arthritis. *Infect Immun*, 67(1), 1999, 173–181.

Allen CS, Franc S, Gary PW, Linden T. Hu, John AB, Joppe WRH, Xin Li, and Paul SM. Lyme borreliosis. *Nat Rev Dis Primers*, 2, 2016, 2, 16090.

Asbrink E, Hovmark A. Classification, geographic variations, and epidemiology of Lyme borreliosis. *ClinDermatol*, 11, 1993, 353-357.

Bacon RM, Kugeler KJ, Mead PS. Centers for Disease Control and Prevention (CDC). Surveillance for Lyme disease--United States, 1992-2006. *MMWR SurveillSumm.*, 57(10), 2008, 01–09.

Behera AK, Durand E, Cugini C. Borreliaburgdorferi BBB07 interaction with integrin alpha3beta1 stimulates production of pro-inflammatory mediators in primary human chondrocytes. *Cell Microbiol*, 10(2), 2008, 320–331.

Benach JL, Bosler EM, Hanrahan JP. Spirochetes isolated from the blood of two patients with Lyme disease. *N Engl J Med*, 308, 1983, 740–742.

Burdge DR, O'Hanlon DP. Experience at a referral centre for patients with suspected Lyme disease in an area of nonendemicity: first 65 patients. *Clin Infect Dis*, 16(4), 1993, 558–560.

Burgdorfer W, Barbour AG, Hayes SF, Benach JL, Grunwaldt E, Davis JP. Lyme disease—a tick-borne spirochetosis? *Science*, 216, 1982, 1317–1319.

CDC estimates of Americans diagnosed with Lyme disease each year. Press release from the Centers for Disease Control and Prevention, 2013.

Chen J, Field JA, Glickstein L. Association of antibiotic treatment-resistant Lyme arthritis with T cell responses to dominant epitopes of outer surface protein A of Borreliaburgdorferi. *Arthritis Rheum*, 42(9), 1999, 1813–1822.

Coburn J, Leong JM, Erban JK. Integrin alpha IIb beta 3 mediates binding of the Lyme disease agent Borreliaburgdorferi to human platelets. *ProcNatlAcadSci U S A*, 90(15), 1993, 7059–7063.

Coburn J, Magoun L, Bodary SC. Integrinsalpha(v)beta3 and alpha5beta1 mediate attachment of lyme disease spirochetes to human cells. *Infect Immun*, 66(5), 1998, 1946–1952.

Coleman JL, Gebbia JA, Piesman J. Plasminogen is required for efficient dissemination of B. burgdorferi in ticks and for enhancement of spirochetemia in mice. *Cell. J*, 89(7), 1997, 1111– 1119.

Dennis DT, Piesman, JF. Overview of tick-borne infections in humans. In: Goodman JL, Dennis DT, Sonenshine DE, eds. Tick-borne infections of humans. Washington, DC. *ASM Press*. 2005.

Derdáková M, Lencáková D. Association of Genetic Variability Within The BorreliaBurgdorferiSensuLato With The Ecology, Epidemiology Of Lyme Borreliosis In Europe. *Ann Agric Environ Med*, 12, 2005, 165-172.

Dressler F, Whalen JA, Reinhardt BN, Steere AC. Western blotting in the serodiagnosis of Lyme disease. *J Infect Dis*, 167(2), 1993, 392–400.

Eugene D. Shapiro, MD. Borreliaburgdorferi (Lyme Disease). *Pedsinreview*, 35(12), 2014, 01-15.

Fikrig E, Feng W, Aversa J. Differential expression of Borreliaburgdorferi genes during erythema migrans and Lyme arthritis. *J Infect Dis*, 178, 1998, 98–1201.

Flisiak R, Pancewicz S. Diagnostics and treatment of Lyme borreliosis. Recommendations of Polish Society of Epidemiology and Infectious Diseases [Polish]. *PrzeglEpidemiol*, 62, 2008, 193-199.

Flisiak R, Prokopowicz D. Antibodies against Borreliagarinii in diagnosis of Lyme borreliosis [Polish]. *PrzeglLek*, 57, 2000, 147-149.

Gasiorowski J, Witecka-Knysz E, Knysz B, Gerber H, Gładysz A. Diagnosis of Lyme disease [Polish]. *Med Pr*, 58, 2007, 439-447.

GrażynaBiesiada, JacekCzepiel, Maciej R. Leśniak, AleksanderGarlicki, Tomasz Mach. Lyme disease: review. *Arch Med Sci*, 8(6), 2012, 978-982.

Gross DM, Steere AC, Huber BT. T helper 1 response is dominant and localized to the synovial fluid in patients with Lyme arthritis. *J Immunol*, 160(2), 1998, 1022–1028.

Guo BP, Brown EL, Dorward DW. Decorin-binding adhesins from Borreliaburgdorferi. *MolMicrobiol*, 30(4), 1998, 711–723.

Hermanowska-Szpakowicz T, Świerzbińska R, Zajkowska J, Iżycka-Herman A. Actual diagnostic possibilities of Lyme borreliosis [Polish]. *Pol MerkLek*, 7, 2000, 69-71.

Hubálek Z, Halouzka J. Distribution of Borreliaburgdorferisensulato genomic groups in Europe, a review. *Eur J Epidemiol*, 13, 1997, 951-957.

John A. Lyme Disease: Symptoms, Causes, Diagnosis, Treatment, Prevention. *Eisen, R. J Med Entomol*, 2016.

Krause A, Brade V, Schoerner C. T cell proliferation induced by Borreliaburgdorferi in patients with Lyme borreliosis. Autologous serum required for optimum stimulation. *Arthritis Rheum*, 34(4), 1991, 393–402.

Lagal V, Postic D, Rubic-Sabljic E, Baranton G: Genetic diversity among Borrelia strains determined by single-strand conformation polymorphism analysis of the ospC gene and its association with invasiveness. *J ClinMicrobiol*, 41, 2003, 5059–5065.

Mullegger RR, McHugh G, Ruthazer R. Differential expression of cytokine mRNA in skin specimens from patients with erythema migrans or acrodermatitischronicaatrophicans. *J Invest Dermatol*, 2000, 1156, 1115–1123.

Nau R, Christen HJ, Eiffert H. Lyme disease – current state of knowledge. *DtschArzteblInt*, 106, 2009, 72-81.

Pal U, de Silva AM, Montgomery RR. Attachment of Borreliaburgdorferi within Ixodesscapularis mediated by outer surface protein A. *J Clin Invest*, 106, 2000, 561–569.

Probert WS, Johnson BJ. Identification of a 47 kDafibronectin-binding protein expressed by Borreliaburgdorferi isolate B31. *MolMicrobiol*, 30(5), 1998, 1003–1015.

Schwan TG, Piesman J, Golde WT. Induction of an outer surface protein on Borreliaburgdorferi during tick feeding. *ProcNatlAcadSci U S A.*, 92, 1995, 2909–2913.

Seinost G, Dykhuizen DE, Dattwyler RJ. Four clones of Borreliaburgdorferisensustricto cause invasive infection in humans. *Infect Immun*, 1999, 67, 3518–3524.

Shapiro ED, Gerber MA. Lyme disease. *Clin Infect Dis*, 31, 2000, 533–542.

Sheila LA and Allen CS.Diagnosis and Treatment of Lyme Arthritis.*Infect Dis Clin North Am*, 29(2), 2015, 269–280.

Stańczak J, Racewicz M, Kubica-Biernat B. Prevalence of Borreliaburgdorferisensulato in Ixodesricinus ticks (Acari, Ixodidae) in different Polish woodlands. *Ann Agric Environ Med*, 6, 1999, 127-32.

Stanek G, Wormser GP, Gray J, Strle F. Lyme borreliosis. *Lancet*, 379, 2012, 461-473.

Steere AC, Coburn J, Glickstein L. The emergence of Lyme disease. *J Clin Invest*, 113, 2004, 1093–1101.

Steere AC, Duray PH, Butcher EC. Spirochetal antigens and lymphoid cell surface markers in Lyme synovitis. Comparison with rheumatoid synovium and tonsillar lymphoid tissue. *Arthritis Rheum*, 31(4), 1988, 487–495.

Steere AC, Grodzicki RL, Kornblatt AN. The spirochetal etiology of Lyme disease. *N Engl J Med*, 308, 1983, 733–740.

Steere AC, Klitz W, Drouin EE. Antibiotic-refractory Lyme arthritis is associated with HLADR molecules that bind a Borreliaburgdorferi peptide. *J Exp Med*, 203(4), 2003, 961–971.

Steere AC, Levin RE, Molloy PJ. Treatment of Lyme arthritis. *Arthritis Rheum*, 37(6), 1994, 878–888.

Steere AC, Malawista SE, Snydman DR. Lyme arthritis: an epi- Lyme arthritis: an epidemic of oligoarticular arthritis in children and adults in three Connecticut communities. *Arthritis Rheum*, 20, 1977, 07–17.

Thomas S. Murray, Eugene D. Shapiro. Lyme Disease. *Clin Lab Med*, 30(1), 2010, 311–328.

Tilly K, Krum JG, Bestor A. BorreliaburgdorferiOspC protein required exclusively in a crucial early stage of mammalian infection. *Infect Immun*, 74, 2006, 3554–3564.

Vincent MS, Roessner K, Sellati T. Lyme arthritis synovial gamma delta T cells respond to Borreliaburgdorferi lipoproteins and lipidatedhexapeptides. *J Immunol*, 161(10), 1998, 5762–5771.

Wormser GP, Dattwyler RJ, Shapiro ED. The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis*, 43, 2006, 1089–1134.

Wormser GP, Nadelman RB, Dattwyler RJ. Practice guidelines for the treatment of Lyme disease. The Infectious Diseases Society of America. *Clin Infect Dis*, 31(suppl 1), 2000, 01-14.

Yin Z, Braun J, Neure L. T cell cytokine pattern in the joints of patients with Lyme arthritis and its regulation by cytokines and anticytokines. *Arthritis Rheum*, 40(1), 1997, 69–79.

Cite this article:
Sangeetha Roy G, Banu Tahrunnisa SK, Mounika S, Sai Krishana K, Rajani Gunnam. Lyme Disease And Its Complications: A Review. *International Journal of Pharmacy & Therapeutics*, 10(1), 2019, 15-23.
DOI: http://dx.doi.org/10.21276/ijpt.2019.10.1.3