Clinical-epidemiologic and serologic characteristics of Lyme disease in the Zaporizhzhia region (a retrospective analysis for 2015–2019 according to the Municipal Institution “Regional Infectious Hospital” of Zaporizhzhia Regional Council)

O. O. Furyk<sup>B,C,D</sup>, K. A. Pak<sup>B, P</sup>, O. V. Riabokon<sup>C,E</sup>, D. A. Zadyraka<sup>D,E</sup>, Yu. Yu. Riabokon<sup>C,D,E</sup>

Zaporizhzhia State Medical University, Ukraine

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

Key words:
Lyme disease, clinic, serodiagnosis.

The aim of the work is to clarify the clinical and laboratory features of Lyme disease in the Zaporizhzhia region on the basis of a retrospective clinical, epidemiological and serological analysis of this disease cases in the period from 2015 to 2019.

Materials and methods. A retrospective analysis of 62 medical cards of stationary patients with Lyme disease for the period from 2015 to 2019 was carried out. The age of the patients ranged from 18 to 79 years. There were 38 men and 24 women. All the patients were given a traditional complex clinical-laboratory examination; ELISA was used to defined serum IgM and IgG to Borrelia burgdorferi.

Results. According to the study results it was found that Lyme disease in the Zaporizhzhia region had a clear seasonal prevalence in summer (56.3 %) and spring (25.8 %). The vast majority of patients (80.6 %) clearly indicated the tick bite. The disease was mostly acute (90.3 %) with a predominance of erythema (94.8 %). In the acute course of the disease, patients were seropositive in 75.0 % of cases with simultaneous detection of both IgM and IgG to Borrelia burgdorferi, and positive IgM in the absence of IgG. Seronegative 25.0 % of patients required clear clinical and epidemiological data to confirm the diagnosis. Under prolonged and chronic conditions, patients had positive IgG to Borrelia burgdorferi (100 %) and IgM (50.0 %).

Certain clinical and laboratory features at different course of Lyme disease were revealed. So, the acute course was characterized by the predominance of erythema (94.8 %), mild or no manifestations of general intoxication syndrome, lack of pathological changes in the hemogram in most patients (80.4 %). In the prolonged and chronic course, there was no history of erythema, clinical symptoms were polymorphic, half of the patients had increased erythrocyte sedimentation rate in the absence of changes in blood count, mild cytolytic syndrome and hyperbilirubinemia.

Conclusions. As a result of the retrospective analysis of Lyme disease cases in the period from 2015 to 2019, certain patterns of epidemiological, clinical and serological changes in different courses of this infection in the Zaporizhzhia region were revealed, namely the clear seasonality of the disease, in the acute course – the predominance of erythema and different variants of serological profile in patients, and in prolonged and chronic course – polymorphism of all clinical symptoms and no history of erythema.
Lyme disease is a naturally occurring bacterial zoonotic infectious disease caused by various genes of the Borrelia complex, characterized by predominant skin lesions in the form of erythema and a tendency to chronicity of the process with damage to the nervous and musculoskeletal systems. Lyme disease remains one of the most common transmissible tick-borne infections in the Northern Hemisphere, with the most common vector being Ixodes spp. [1,2].

The morbidity of Lyme disease in the world has been growing steadily over the past two decades [3]. According to the Centers for Disease Control and Prevention (CDC), about 300,000 cases are reported annually in the United States [4]. In the European region, the highest incidence is recorded in Central and Northern Europe, as well as in the Baltic countries [3,5]. In Ukraine, in 2019, 4482 cases were registered [6]; in 2019, the overall incidence in the Baltic countries [3,5]. In Ukraine, in 2019, 4482 cases were registered [6]; in 2019, the overall incidence in the Baltic countries [3,5]. In Ukraine, in 2019, 4482 cases were registered [6]; in 2019, the overall incidence in the Baltic countries [3,5].

Clinical diagnosis of Lyme disease has significant difficulties due to the polymorphic clinical manifestations of the disease, which in turn depends on the characteristics of a causative pathogen, and the clinical form and stage of the disease. It is known that the causative agent of Lyme disease is often one of three genes: Borrelia burgdorferi sensu stricto, B. afzelii and B. garinii [9,10]. However, other genes, such as B. bissettiae, B. lusitanae, B. spielmanii, and B. valaisiana, have recently been reported, mainly in Europe [11]. The geographical distribution and heterogeneity of the pathogen determine certain differences in clinical manifestations due to the specificity of the pathogen by the source of infection and tropism to target organs. Borrelia burgdorferi sensu stricto is distributed mainly in North America and is associated with neuroborreliosis [12], B. afzelli, B. garinii, B. burgdorferi, B. spielmanii and B. bavariensis are common in Asia and Europe [13], neuroborreliosis is associated with B. garinii, and chronic skin lesions, including chronic acrodermatitis attributed to B. afzelli [10].

In addition, polymorphic clinical manifestations of Lyme disease depend not only on the heterogeneity of the pathogen, but also on the stage of the process. The early localized stage is characterized by the presence of migrating erythema in the site of a tick bite; however, erythema is absent in at least 20% of cases [14]. Therefore, even the general intoxication syndrome, which occurs at this stage in some patients, in the absence of erythema or in the presence of non-standard clinical variations, leads to diagnostic errors [15,16].

If Lyme disease is not diagnosed at an early stage, the pathogen is disseminated early hematogenously or lymphogenously with the involvement of various target organs in the pathological process. Therefore, in addition to general intoxication, patients develop various multisystem lesions, such as multifocal migratory erythema, benign lymphocytoma of the skin, meningitis, encephalitis, polyradiculoneuropathy, neuritis or facial nerve neuropathy, carditis. Further progression of Lyme disease is characterized by the formation of late disseminated stage, which is most often clinically manifested by progression of neurological disorders, chronic atrophic skin lesions, large joint oligoarthritis due to autoimmune and immunopathological reactions [17,18]. All this further complicates not only the diagnosis of this disease, but also significantly reduces the effectiveness of etiotropic treatment.

Therefore, the above necessitates the analysis of clinical, epidemiological and laboratory features of Lyme disease in the Zaporizhzhia region, that would determine certain patterns of this infection and improve early diagnosis.

**Aim**

The aim of the work is to clarify the clinical and laboratory features of Lyme disease in the Zaporizhzhia region on the basis of a retrospective clinical, epidemiological and serological analysis of this disease cases in the period from 2015 to 2019.

**Materials and methods**

A retrospective analysis of 62 medical records of inpatients with Lyme disease (A 69.2), who were examined and treated in the departments of the Municipal Institution “Regional Infectious Diseases Clinical Hospital” of the Zaporizhzhia Regional Council for the period from 2015 to 2019. The age of patients ranged from 18 to 79 years, the mean age was 46.1 ± 2.2 years. There were 38 men and 24 women.

All the patients with Lyme disease underwent a traditional comprehensive clinical and laboratory examination at the hospital, and ELISA were performed to determine serum IgM and IgG to Borrelia burgdorferi. The course of Lyme disease was evaluated according to the recommendation [19], based on which the early period (including stages of local infection and dissemination) and the late period (stage of persistent infection) was defined. Depending on the nature of the course, there were acute course (up to 3 months), subacute course (up to 6 months) and chronic (prolonged or recurrent) course.

Statistical data processing was performed using the program Statistica 13 for Windows (StatSoft Inc., No. JPZ8041382130ARCN10-J).
Results

According to the results of the epidemiological anamnensis, it was found that Lyme disease in the Zaporizhzhia region has a clear seasonality with a predominance of patients in summer (n = 35, 56.5 %) and spring (n = 16, 25.8 %). It should be noted that in autumn, the number of patients decreased rapidly (n = 10, 16.1 %), and in winter, there were only 1 (1.6 %) case of this infection during the entire observation period (Fig. 1).

The vast majority of patients (n = 50, 80.6 %) in the epidemiological history clearly indicated the tick bite when visiting various natural sites. It is worth noting that none of persons sought medical help after the tick bite and, accordingly, they did not receive urgent post-exposure prophylaxis.

Analysis of the clinical course showed that Lyme disease was mostly acute (n = 56, 90.3 %), in some cases prolonged (n = 2, 3.2 %) and chronic (n = 4, 6.5 %). The disease mainly was moderate (n = 53, 85.5 %), 9 (14.5 %) patients had a mild course, patients with severe Lyme disease during the study period was not detected.

The analysis of serological tests for IgM and IgG to Borrelia burgdorferi showed that all patients with prolonged (>3 months) and chronic (>6 months) Lyme disease were seropositive for IgG to Borrelia burgdorferi, and every second patient was positive for both IgM and IgG. However, patients with acute Lyme disease who were examined on average on day 23.7 ± 2.3 of the disease demonstrated certain features of the serological profile in the study of different classes of antibodies to Borrelia burgdorferi. During this period of examination, 75.0 % (42 of 56) patients with acute disease were seropositive, patients with positive both IgM and IgG to Borrelia burgdorferi (n = 22, 39.3 %) were detected with the same frequency, and patients with positive IgM to Borrelia burgdorferi in the absence of IgG to the pathogen accounted for 35.7 % (n = 20). Seronegative was one of the four patients (n = 14, 25.0 %) with acute Lyme disease (Fig. 2). Therefore, it should be noted that the basis for confirmation of the diagnosis in these cases were clinical and epidemiological data, namely epidemiological history of tick bite a few days or weeks before the onset of clinical manifestations, in addition, erythema was diagnosed in all these patients with Lyme disease.

In the analysis of clinical variants of acute Lyme disease, a clear prevalence of erythema was detected – in 94.6 % (53 of 56) of patients, and in 5.7 % (3 of 53) of cases, the prevalence of erythema was combined with joint damage. In patients with erythema, lesions were most commonly localized on the skin of the lower (n = 29, 54.7 %) and upper extremities (n = 9, 17.0 %), less often – on the skin of the trunk, namely on the skin of the anterior surface of the chest (n = 6, 11.3 %) and the anterior abdominal wall (n = 5, 9.4 %), lumbar skin (n = 2, 3.8 %), scrotal skin (n = 1, 1.9 %), and the presence of erythema was recorded on the skin around the ear in 1 (1.9 %) case. The size of the formed erythema varied in a wide range with a diameter from 2.5 cm in the formation of annular erythema to 40 cm in cutaneous manifestations in the form of migrating erythema. At the same time, 17.0 % (9 of 53) of patients with erythema experienced moderate itching of the skin at the site of erythema. It was noteworthy that in patients with erythematous Lyme disease, signs of general intoxication syndrome were either absent or manifested in some patients by short-term subfebrile temperature (n = 3, 5.7 %) and moderate weakness (n = 5, 9.4 %).

In the acute course of the disease, the erythema-free form was recorded in 5.4 % (3 of 56) of patients. The development of this form was accompanied by the appearance of moderate general intoxication syndrome due to subfebrile temperature, asthenovascular manifestations, and one case was accompanied by damage to the joints and central nervous system in the form of serous meningitis. Given the absence of erythema characteristic of this infection in all patients with erythematous form, the diagnosis of Lyme disease was serologically confirmed by the detection of IgM and IgG to Borrelia burgdorferi during a comprehensive diagnostic examination. It is also noteworthy that patients with acute Lyme disease, despite the prevalence of erythema, were hospitalized in the third week after the onset of clinical manifestations.

Analysis of general clinical data from laboratory studies in patients with acute Lyme disease showed that most patients (n = 45, 80.4 %) had no pathological changes in the hemogram. However, in 7 (12.5 %) patients, leukopenia was found from 3.7 × 10⁹/l to 2.0 × 10⁹/l, averaging up to (2.96 ± 0.29) × 10⁹/l, in 4 (7.1 %) patients, on the contrary, leukocytosis ranged from 9.0 × 10⁹/l to 13.8 × 10⁹/l, averaging up to (11.6 ± 0.37) × 10⁹/l. At the same time,
ectoparasite that can easily go unnoticed when attached to stage as well as the adult stage of the vector, is a small and epidemiological data. However, the immature nymphal in practical medicine [21].

Discussion

It is known that the diagnosis of Lyme disease is based on clinical and epidemiological data and serological diagnosis. Lyme disease is characterized by spring–autumn seasonality, which is associated with the activity of the vector, the peak number of cases occurs in the summer months [17,20]. According to the results of our analysis, a clear seasonality of Lyme disease in the Zaporizhzhia region was also established, with a predominance of patients in summer (56.5 %) and spring (25.8 %). It is considered important to diagnose Lyme disease at an early stage of the process, as untimely or lack of antibiotic therapy leads not only to dissemination of the process, but also to serious complications and negative prognosis for recovery and quality of life [4,21,22]. Despite the growing awareness of clinicians about Lyme disease over the past decade, errors in clinical and specific diagnosis are quite common in practical medicine [21].

Early diagnosis of Lyme disease is based on clinical and epidemiological data. However, the immature nymphal stage as well as the adult stage of the vector, is a small ectoparasite that can easily go unnoticed when attached to humans, which in combination with nonspecific symptoms of Lyme disease and the absence of migratory erythema can lead to delays in diagnosis or misdiagnosis [23]. According to the analysis of Lyme disease cases in the Zaporizhzhia region, it was found that only 80.6 % of patients clearly indicated the tick bite, almost one in five patients could not remember the tick bite. At the same time, in the conditions of prolonged or chronic course in patients, there was no history of erythema, clinical symptoms were polymorphic with a predominance of astheno-vegetative manifestations, varying intensity of arthralgia, low-grade fever, headache and other. If clinical and epidemiological data were sufficient to confirm the erythematous form of Lyme disease, all other clinical variants of this infection required mandatory laboratory confirmation.

The specific laboratory diagnosis of Lyme disease remains difficult. To date, the inexpediency of using bacteriological examination due to low sensitivity and slow growth of the pathogen has been proven [1,15,24,25]. Diagnosis of Lyme disease remains challenging even with the help of molecular genetic methods, because the sensitivity depends on the type and volume of biological material sample, the presence of polymerase chain reaction inhibitors due to contamination [26]. The sensitivity of the polymerase chain reaction in the diagnosis of Lyme disease varies from 34 % to 64 % [27,28].

During the low sensitivity, technical complexity and time constraints of direct methods, most European and US countries use a two-level protocol for serological diagnosis of Lyme disease [2]. In the first stage, ELISA detect antibodies to pathogen antigens [9]. In case of doubtful result of ELISA in the second stage, a highly specific immunological method (immunoblotting) is used to check the presence of antibodies to specific Borrelia proteins [24,28]. The disadvantage of this protocol is the relatively low sensitivity of 25 % to 50 % in the early stages of the disease, because the synthesis of sufficient antibodies to identify them in the blood takes at least three weeks. In addition, in the early period of the disease, false-negative results are often found due to cross-reactions in the presence of autoimmune, rheumatic, hematological and some other infectious diseases [1,29]. In the later stages, when antibody titers increase due to the activity of B-lymphocytes, the sensitivity of this examination increases to 99 % [28,30].

According to the results analyzing our serological examinations, patients with prolonged and chronic Lyme disease had positive IgG to Borrelia burgdorferi (100 %) and IgM in 50.0 % of cases. However, in patients with acute Lyme disease, serological confirmation of the diagnosis was obtained in 75.0 % of simultaneous detection of both IgM and IgG to Borrelia burgdorferi (39.3 %) and positive IgM in the absence of IgG (35.7 %). Obtained seronegative results in 25.0 % of patients with acute Lyme disease required clear clinical and epidemiological data to confirm the diagnosis.

Conclusions

1. Lyme disease in the Zaporizhzhia region has a clear seasonality with a predominance of patients in summer (56.5 %) and spring (25.8 %). The vast majority of patients (80.6 %) clearly indicated the tick bite when visiting various
natural sites. The disease was mostly acute (90.3 %) with a predominance of erythema (94.6 %), in some cases there was the prolonged (3.2 %) and chronic (6.5 %) course.

2. The serological profile of patients with acute Lyme disease was characterized by seropositivity of 75.0 % with simultaneous detection of both IgM and IgG to *Borrelia burgdorferi* (39.3 %) and positive IgM in the absence of IgG (35.7 %). Seronegative 25.0 % of patients required clear clinical and epidemiological data to confirm the diagnosis. Patients with prolonged and chronic Lyme disease had positive IgG to *Borrelia burgdorferi* (100 %) and IgM in 50.0 % of cases.

3. Acute Lyme disease was characterized by a predominance of erythema (94.6 %) with the most common localization on the skin of the lower (54.7 %) and upper extremities (17.0 %), mild or no manifestations of general intoxication syndrome, lack of pathological changes in the hemogram in most patients (80.4 %), and if there were any, it was leukopenia (12.5 %) or leukocytosis (7.1 %) with the presence of lymphocytosis (19.6 %) and accelerated ESR (17.9 %).

4. In the case of prolonged and chronic Lyme disease, there was no history of erythema, clinical symptoms were polymorphic and included asthenic-vegetative manifestations, varying intensity of arthralgia, low-grade fever, loss of appetite, headache, discomfort in the heart, decreased visual acuity. Half of the patients had the accelerated ESR in the absence of changes in blood count, mild cytolytic syndrome and moderate hyperbilirubinemia.

**Conflicts of interest:** authors have no conflict of interest to declare.

**Конфлікт інтересів:** відсутній.

**References**

[1] Schutzer, S. E., Body, B. A., Boyle, J., Branson, B. M., Datwyler, R. J., Fikrig, E., Gerald, N. J., Gomes-Solecki, M., Kintup, M., Ledzit, M., Levin, A. E., Lewinski, M., Liotta, L. A., Marques, A., Mead, P. S., Mondongin, E. F., Pillai, S., Rao, P., Robinson, W. H., Roth, K. M., ... Brandt, J. A. (2019). Direct Diagnostic Tests for Lyme Disease. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America, 68(6), 1052-1057. https://doi.org/10.1093/cid/ciy614

[2] Steere, A. C., Stire, F., Wormser, G. P., Hu, L. T., Brandt, J. A., Hovius, J. W. R., Li, X., Mead, P. S. (2016). Lyme borreliosis. Nature Reviews Disease Primers, 2. https://doi.org/10.1038/nrdp.2016.50

[3] Sykes, R. A., & Makiello, P. (2017). An estimate of Lyme borreliosis incidence in Western Europe. Journal of public health, 39(1), 74-81. https://doi.org/10.1093/jpubhj/jwx017

[4] Centers for Disease Control and Prevention (2013, Aug 19). CDC Provides Estimate of Americans Diagnosed with Lyme Disease Each Year. http://www.cdc.gov/media/releases/2013/20130819-lyme-disease.html

[5] Mead, P. S. (2015). Epidemiology of Lyme disease. Infectious disease clinics of North America, 29(2), 187-210. https://doi.org/10.1016/j.idc.2015.02.010

[6] Center for Public Health of the Ministry of Health of Ukraine (2020, May 5). Za try miissiat $2020-30 roky v Ukraini zaafiksovan 236 vyvistik khvoroby Laima [In three months of 2020, 236 cases of Lyme disease were recorded in Ukraine]. https://iph.gov.ua/news/za-tri-missiati-2020-go-roku-v-ukraini-zafiikovalo-236-vyvistik-khvoroby-laima

[7] Nebogatkin, I. V., & Shulman, A. M. (2021). Epidemiologichni y epizootichni osoblyvosti khvoroby Laima u 2019 roty v Ukraini [Epidemiological and epizootic features of Lyme disease in 2019 in Ukraine]. Aktualna infektolohiia, 8(5-6), 44-48. [in Ukrainian]. https://doi.org/10.12941/1734-4313/8.5-6-2020.217923

[8] Stone, B. L., Touard, Y., & Briquette, C. A. (2017). Brave New Worlds: The Expanding Universe of Lyme Disease. Vector borne and zoonotic diseases, 17(9), 619-629. https://doi.org/10.1093/vbz/17.9.619

[9] Cardenas-de la Garza, J. A., De la Cruz-Valadez, E., Ocampo-Candiani, J., & Welsh, O. (2019). Clinical spectrum of Lyme disease. European journal of clinical microbiology & infectious diseases, 38(2), 201-208. https://doi.org/10.1007/s10096-018-3417-1

[10] Stojadinovic, P., Lemic, M., Trojanovski, V. P., & Stojadinovic, O. (2018). Lyme Borreliosis in North America. Frontiers in medicine, 5. https://doi.org/10.3389/fmed.2018.00023

[11] Estrada-Peña, A., Cutler, S., Potkonjak, A., Vassier-Tussaut, M., Strnad, M., Hönig, V., Růžek, D., Grubhoffer, L., & Rego, R. (2017). serol onal analysis of the distribution and prevalence of *Borrelia burgdorferi* s.l. in ticks in Europe. International journal of health geographics, 17(1). https://doi.org/10.1186/s40242-018-0183-7

[12] Pritt, B. S., Mead, P. S., Johnson, D., Netzel, D. F., Respicio-Kingry, L. B., Davis, J. P., Schiffman, E., Sloan, L. M., Schriefer, M. E., Replogle, A. J., Paskewitz, S. M., Ray, J. A., Bjork, J., Steward, C. R., Deedon, L. B., ... Shapiro, E. D. (2014). Lyme disease. The New England Journal of Medicine, 370(14), 1324-1337. https://doi.org/10.1056/NEJMcp1314325

[13] Moore, A., Nelson, C., Molins, C., Mead, P., & Schriefer, M. (2016). Current Guidelines, Common Clinical Pitfalls, and Future Directions for Laboratory Diagnosis of Lyme Disease, United States. Emerging infectious diseases, 22(7), 1169-1177. https://doi.org/10.3201/eid2207.151694

[14] Sharma, A., Guliera, S., Sharma, R., & Sharma, A. (2017). Lyme Disease: A Case Report with Typical and Atypical Lesions. Indian dermatology online journal, 9(2), 124-127. https://doi.org/10.4103/2229-5178.202271

---

**Information about authors:**

Furyk O. O., MD, PhD, Associate Professor of the Department of Infectious Diseases, Zaporozhye State Medical University, Ukraine. ORCID ID: 0000-0002-5196-7698

Pak K. A., MD, Senior Laboratory Assistant of the Department of Infectious Diseases, Zaporozhye State Medical University, Ukraine. ORCID ID: 0000-0002-2286-6919

Riabokon O. V., MD, PhD, DSc, Professor, Head of the Department of Infectious Diseases, Zaporozhye State Medical University, Ukraine. ORCID ID: 0000-0002-7394-4649

Zadyraka D. A., MD, PhD, Associate Professor of the Department of Infectious Diseases, Zaporozhye State Medical University, Ukraine. ORCID ID: 0000-0003-3970-9140

Riabokon Yu. Yu., MD, PhD, DSc, Professor of the Department of Children Infectious Diseases, Zaporozhye State Medical University, Ukraine. ORCID ID: 0000-0002-2273-8511

---

**Відомості про авторів:**

Фур'єк О. О., харк., мед. наук., доцент каф. інфекційних хвороб, Запорізький державний медичний університет, Україна. Пак К. А., старший лаборант каф. інфекційних хвороб, Запорізький державний медичний університет, Україна.
National Institute for Health and Care Excellence. (2018, October 17). Lyme disease NICE guideline [NG95]. https://www.nice.org.uk/guidance/ng95

Rebman, A. W., & Aucott, J. N. (2020). Post-treatment Lyme Disease as a Model for Persistent Symptoms in Lyme Disease. Frontiers in medicine, 7, 7F. https://doi.org/10.3389/fmed.2020.00057

Chemych, M., & Lutai, I. (2020). Lyme disease modern issue condition. Eastern Ukrainian Medical Journal, 8(2), 230-241. [In Ukrainian]. https://doi.org/10.21272/eumj.2020.8(2).230-241

Tulloch, J., Decraene, V., Christley, R. M., Radford, A. D., Warner, J. C., & Vivancos, R. (2019). Characteristics and patient pathways of Lyme disease patients: a retrospective analysis of hospital episode data in England and Wales (1998-2015). BMC public health, 19(1), 931. https://doi.org/10.1186/s12889-019-7245-8

Hirsch, A. G., Herman, R. J., Rebman, A., Moon, K. A., Aucott, J., Heaney, C., & Schwartz, B. S. (2018). Obstacles to diagnosis and treatment of Lyme disease in the USA: a qualitative study. BMJ open, 8(5), e021367. https://doi.org/10.1136/bmjopen-2017-021367

Knudtzen, F. C., Andersen, N. S., Jensen, T. G., & Skarphédinsson, S. (2017). Characteristics and clinical outcome of Lyme neuroborreliosis in a high endemic area, 1995-2014: a retrospective cohort study in Denmark. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America, 65(6), 1489-1495. https://doi.org/10.1093/cid/cix568

Kannangara, D. W., & Patel, P. (2018). Report of non-Lyme, erythema migrans rashes from New Jersey with a review of possible role of tick salivary toxins. Vector borne and zoonotic diseases, 18(12), 641-652. https://doi.org/10.1089/vbz.2018.2279

 Eldin, C., Jaulhac, B., Mediannikov, O., Arzouni, J. P., & Raoult, D. (2019). Values of diagnostic tests for the various species of spirochetes. Medicine et maladies infectieuses, 49(2), 102-111. https://doi.org/10.1016/j.medmal.2019.01.002

Sanderson, V. P., Mainprize, I. L., Verzijlenberg, L., Khursigara, C. M., & Wills, M. (2020). The platelet fraction is a novel reservoir to detect Lyme Borrelia in blood. Biology, 9(11), 366. https://doi.org/10.3390/biology9110366

Lacout, A., Mone, Y., Franck, M., Marcy, P. Y., Mas, M., Veas, F., & Perronne, C. (2018). Blood cell disruption to significantly improve the Borrelia PCR detection sensitivity in borreliosis in humans. Medical hypotheses, 116, 1-3. https://doi.org/10.1016/j.mehy.2018.04.012

Rubel-Sabljic, E., & Cerar, T. (2017). Progress in the molecular diagnosis of Lyme disease. Expert review of molecular diagnostics, 17(1), 19-30. https://doi.org/10.1080/14737159.2016.1248696

Waddell, L. A., Greig, J., Mascarenhas, M., Harding, S., Lindsay, R., & Ogden, N. (2016). The Accuracy of Diagnostic Tests for Lyme Disease in Humans, A Systematic Review and Meta-Analysis of North American Research. PloS one, 11(12), e0168613. https://doi.org/10.1371/journal.pone.0168613

Maccallini, P., Bonini, S., & Trevisan, G. (2018). Autoimmunity against a glycolytic enzyme as a possible cause for persistent symptoms in Lyme disease. Medical hypotheses, 710, 1-8. https://doi.org/10.1016/j.mehy.2017.10.024

Crossland, N. A., Alvarez, X., & Embers, M. E. (2018). Late disseminated Lyme disease: Associated Pathology and Spirochete persistence Post-treatment in rhesus macaques. The American journal of pathology, 188(3), 672-682. https://doi.org/10.1016/j.ajp.2017.11.055