

## THE ANALYSIS OF THE COURSE OF EARLY LOCALIZED LYME DISEASE AMONG PATIENTS OF THE INFECTIOUS DISEASES CLINIC IN SZCZECIN

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**Abstract.** Lyme disease (also known as borreliosis) is defined as an infectious disease caused by a spirochete called *Borrelia burgdorferi*. It occurs in three stages: early localized infection, early disseminated infection and late persistent infections that affect many organs. In order to assess the clinical course, including the transition to the late persistent infection stage, medical records of a group of 175 patients, who reported at the Infectious Disease Clinic in Szczecin after treating chronic erythema in 2004, were analyzed. Clinical symptoms, presence of serological exponents and frequency of transition into the late persistent infection stage were assessed. In majority of the observed patients, the infection was limited to erythema migrans. Average time, in which serological negativization in the IgM class occurred was 13.2 months, 15 people throughout the observation time showed the presence of antibodies in the IgM class, which were not associated with clinical exponents of the disease. In 8 patients (4.6%) the infection turned into a chronic-arthral form. Lyme borreliosis, when properly treated and taken care of in the first stage, rarely becomes a chronic disease.

**Key words:** antiborreliosis antibodies, *Borrelia burgdorferi*, chronic Lyme disease, erythema migrans, Lyme disease

### INTRODUCTION

*Borrelia* spirochetes infection is very common in the Northern Hemisphere. In terms of clinical symptoms, it may manifest itself as a disease of diverse sympto-

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matology lasting from a few weeks up to many years. Reservoirs of spirochetes that cause Lyme borreliosis are wild animals, which are the source of infection for ticks that are carriers of this bacterium. In Poland, these ticks are *Ixodes ricinus* and *Ixodes persulcatus* [Flisiak 2012].

In the course of the disease, the infected areas include the skin, the osteoarticular, nervous, and circulatory systems. Other organs, such as eyes, kidneys and liver are rarely affected. Pathomechanism of changes is associated with the bacteria-induced inflammation, but also with autoimmune phenomena, as it is postulated in borrelia arthritis [Flieger 2001, Burrascano 2008].

The diverse clinical picture of Lyme disease, and an eventual chronic nature of the disease, is affected by the existence of more than one genospecies of bacteria of diverse tissue tropism, reaction of the host and the use, or absence, of antibiotics in the early stages of the infection [Flisiak and Pancewicz 2008, Flisiak 2012]. In Europe, there are at least three genospecies of spirochete pathogenic for humans. They show certain clinical predispositions: *B. burgdorferi sensu stricto* with a predisposition to cause arthral forms of borreliosis, *B. garinii* with a predisposition to affect the nervous system, and *B. afzelii* that causes chronic problems with atrophic dermatitis of the limbs [Steere 2010, Grzeszczuk 2009].

Data on the clinical course, including the frequency of transition into the chronic stage of the disease and the rate of affecting particular systems and organs, is very divergent. The risk of disease acquisition is related to the frequency of tick infection in the given region and is increased after a bite of the soft skin, when the time of the contact exceeds 24–48 hours [Flisiak and Szechiński 2006].

The most common symptom in Lyme disease is erythema migrans, which is a consequence of bacterial inoculation by infected ticks. Moreover, it is the only pathognomonic change in Lyme disease [Flisiak and Szechiński 2006, Flisiak 2012, Biesiada et al. 2012]. It is classified as an early and localized form of the disease, as well as the much less common Lymphadenitis benigna Curtis – LBC. Erythema migrans shows itself in the tick bite region after 1–3 weeks, but up to 3 months may pass until it is fully exposed. Furthermore, erythema migrans can be diagnosed when the change grows as days go by and exceeds the diameter of 5 cm [Flisiak and Pancewicz 2008, Grzeszczuk 2009].

Other forms of the disease – arthritis, myocarditis, radiculitis, meningitis related to spread of the pathogen through blood or lymph, are unspecific and require careful differentiation and confirmation of infection over laboratory methods [Zajkowska 2000]. They are observed both in a form of early and late spread infections.

Patients with Lyme disease have affected one or more organs and systems, which combined with a lack of clear diagnostic methods, can lead to a so-called

overdiagnosis of Lyme disease. However, sometimes it may delay a proper diagnosis and treatment [Gąsiorowski et al. 2007].

Due to divergent literature data on the course of the disease, the history of infection with *Borrelia burgdorferi* was analyzed based on own material – research data taken from patients of the Infectious Diseases Clinic at the Independent Public Provincial Hospital (*SPWSZ – Samodzielny Publiczny Wojewódzki Szpital Zespolony*) in Szczecin. This research study aimed at assessing the course of infection, including clinical symptoms and serological exponents with the frequency of transition into the chronic stage in patients treated with antibiotics at the erythema migrans stage.

## **MATERIAL AND METHODS**

The study was conducted based on an analysis of medical records of 175 patients reported at the Infectious Diseases Clinic in Szczecin (113 women, 66 men) aged 18–83 (average 48.95,  $\pm 12.95$ ), who were diagnosed with chronic erythema in 2004.

The observations included patients whose lesion size exceeded 5 cm in diameter and lasted for a long time. Patients in whom the clinical symptoms of chronic erythema were hard to diagnose were excluded from the observation.

The subjects were observed from 3 up to 48 months. Eight people are still under the care of the Infectious Diseases Clinic. Every subject suffered from signs and symptoms that, in addition to the skin, could indicate problems to other systems or organs. The patients were informed of possible symptoms associated with chronic or protracted *B. burgdorferi* infection in order to report to further research.

Most of the patients were subjected to serological tests for the presence of anti-*Borrelia* antibodies to detect seroconversion, duration of humoral response and type of antibodies. The first serological tests over the enzyme-linked immunosorbent assay method (ELISA), the Euroimmun test, were conducted at an interval of 1 up to 12 months after diagnosing chronic erythema. After obtaining positive results, or in a situation of finding symptoms of chronic Lyme disease, the studies were repeated during subsequent visits. For statistics (mean, standard deviation, median) Statistica 8.0 PL software was used.

## **RESULTS**

The largest group among the subjects was constituted by urban residents, mostly women (65%). The average incidence age was 48.95 years. Only 11 of the subjects

had a job associated with an increased risk of exposure to ticks (foresters, farmers) (Table 1).

Table 1. Characteristics of the patients

Tabela 1. Charakterystyka chorych

Characteristic of the patients Charakterystyka chorych	Results Wyniki	Percentage share Udział procentowy %	Standard deviation Odchylenie standardowe ±SD
Number of patients Liczba chorych	175		
Average age in years Średni wiek w latach	48.95		±12.95
Gender – male/female Płeć – mężczyźni/kobiety	62/113	35/65	
Dwelling place – city/village Miejsce zamieszkania – miasto/wieś	145/30	82.9/17.1	
Average treatment time of erythema in days Średni czas trwania leczenia rumienia w dniach	19.32		±6.86
Average time interval between the occurrence of erythema to conducting the first serological examination in months Średni odstęp czasu od wystąpienia rumienia do wykonania 1. badania serologicznego w miesiącach	5.32		±2.51
Number of patients with occupational risk of infection Liczba chorych z ryzykiem zawodowym zakażenia	11	6.3	

Most of the patients, 89.7%, were treated when chronic erythema was diagnosed. The most frequent treatment method included tetracycline (doxycycline) or amoxicillin. Several patients received azithromycin or cefuroxime axetil. One person was treated with Bisepitol, one with phenoxymethyl penicillin, and one with ceftriaxone. Twenty people did not remember the name of the antibiotic they had been given. The average treatment duration was 19.32 days (the shortest was five days, the longest 10 weeks).

Serological studies after treating erythema migrans were conducted in 172 people – three did not report for observation. The average time from the incidence of erythema to the first serological test for the presence of anti-*Borrelia* antibodies was 3.52 months (SD ±2.51). Among the subjects, 85 patients (49%) were negative for antibodies in every class; 55 patients (31%) had IgM antibodies; 12 (7%) had IgG antibodies; 14 (8%) had a limit value and in 6 (3%) the presence of antibodies in both classes – IgG and IgM – was observed (Fig. 1).

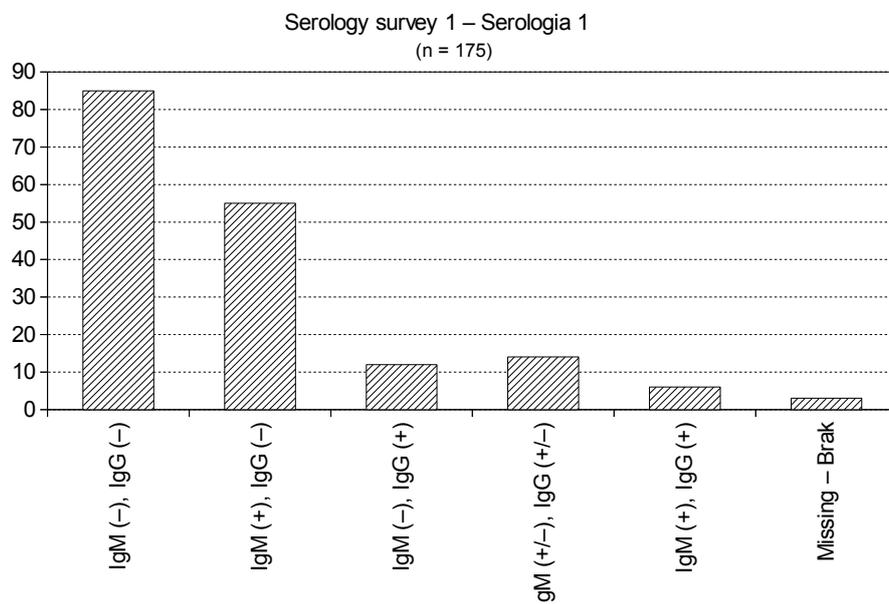


Fig. 1. Percentage of people positive serum values among the patients after treating erythema migrans (the first examination)

Rys. 1. Odsetek osób surowiczododatnich wśród badanych po leczeniu rumienia wędrującego (badanie pierwsze)

Further observations included patients diagnosed with the presence of antibodies in the IgM, IgG, or both classes as well as patients who had experienced problems with the motor system or other difficulties which could correspond to other forms of Lyme disease: muscle pain, arthritis, influenza-like or root-like symptoms, which could not be attributed to a different aetiology. Predominant symptoms were joints pain, especially the limbs.

The average time between the detection of serum antibodies to their disappearance was 13.2 months (minimum 3 months, maximum 48 months). In 15 of the subjects, throughout the whole course of the examination, the presence of antibodies in the IgM class and negative antibodies in the IgG class were observed. No clinical exponents of infection were found (Fig. 2).

In the analyzed group of 175 people, only 8 subjects (4.6%) had progression of the infection to chronic Lyme disease – in all cases it was arthritis. The diagnosis of chronic Lyme disease was based on the occurrence of the aforementioned symptoms that lasted more than 12 months with the appearance of antibodies in the IgG class which had not been found before. Those patients were treated with antibiotics again.

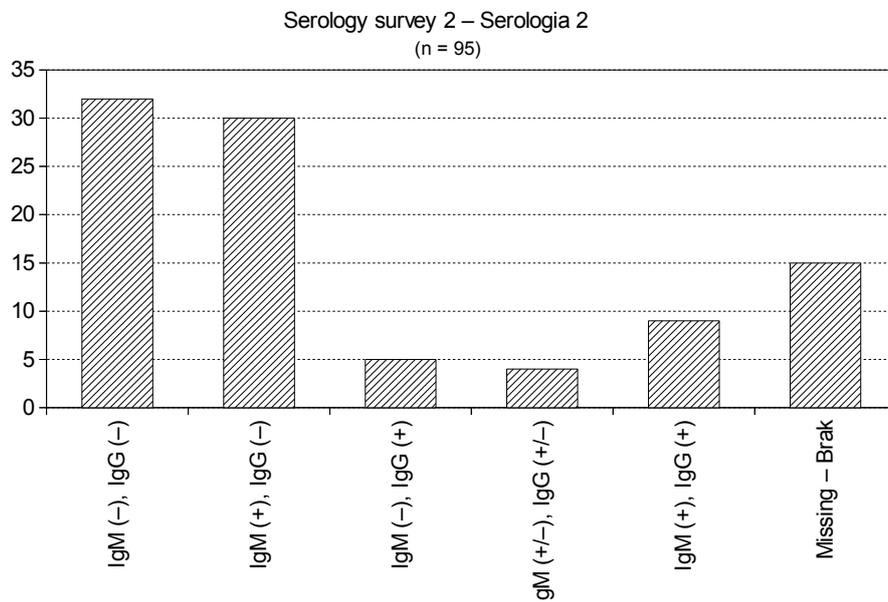


Fig. 2. The presence of anti-*Borelia* antibodies – the second examination. The patients with positive serology in the first examination were examined

Rys. 2. Obecność przeciwciał anti-*Borelia* – badanie drugie. Badani byli pacjenci z dodatnią serologią boreliozy w pierwszym badaniu

## DISCUSSION

Despite the fact that it has been more than thirty years since Lyme disease was defined, there is still controversy regarding diagnostic criteria or treatment standards for this disease. The latter issue – Lyme disease treatment – is very problematic of late [Stricker and Johnson 2008].

In many publications, some scientists argue that Lyme disease is difficult to treat or even untreatable, the proof of which is the long-term presence of antibodies against antigens *B. burgdorferi* in serum or fragments of genetic material of the bacteria detected over PCR methods in different tissues.

Other medical circles, including the Infectious Diseases Society of America, believe that the course of this infection is similar to other bacterial diseases and can be treated with suitable treatment methods. Repeatable antibiotic treatments are recommended only if the chronic (late) stage of infection can be documented.

According to the IDSA, health complaints that persist after treatment are treated as an after-borreliosis syndrome which should not be treated with antibiotics.

However, the second group of doctors, led by the International Lyme and Associated Diseases Society (ILADS), recommends an aggressive, long-term and multi-drug therapy [Burrascano 2008].

The results of our observations suggest that there is a connection between starting an early treatment and eliminating the infection, which is consistent with the position taken by the IDSA. Majority of the patients did not suffer from any other forms of infection, except for erythema migrans. Chronic Lyme disease was diagnosed in only eight of the 175 of the patients (4.6%). The low percentage of those patients was probably the result of a rapid implementation of the treatment – at the early localized infection stage. On the other hand, the occurrence of chronic Lyme disease, despite the treatment, forces to analyze the causes of this situation – an inappropriate antibiotic therapy or a too short treatment time.

The presence of antibodies in the IgM class, more seldom IgG, after treating erythema migrans was observed in less than half of the subjects. Once again, this confirms the official opinion on the diagnosis of erythema (quoted) that the serological test is unnecessary when dealing with typical skin lesions for economic reasons and the fact that in half of the subjects it can be negative [Niścigorska 1996].

Frequency of *Borrelia burgdorferi* infection in the West-Pomeranian region of Poland was previously assessed based on the immunoserological tests in the population of forest workers. In this group high prevalence of the *Borrelia burgdorferi* infection was noted, with no correlation observed between age, duration of employment as the forestry worker and presence of anti-Borrelial antibodies. Frequency of these infections in various Polish forest superintendencies was similar.

Of note, the presence of anti-*Borrelia* antibodies in the IgM class when the disease does not progress – that is, clinical changes and antibodies in the IgG class do not occur – lasts for a long time. The presence of persistent antibodies in the IgM class averaged over a year, and in extreme cases – four years. This shows that when establishing a treatment method based on results of serological tests and absence of evident clinical data, due caution is advised.

## CONCLUSIONS

1. Implementation of antibiotic treatment at the erythema migrans stage gives a great chance to eliminate the infection and prevent chronic Lyme disease.
2. Chronic Lyme disease can develop in a few percent of patients despite treating the early infection.
3. In some patients with chronic erythema, the presence of persistent antibodies in the IgM class is observed. They can occur up to several years; their

presence in the absence of clinical data should not be the basis for unjustified repeated therapies.

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**ANALIZA PRZEBIEGU KLINICZNEGO WCZESNEJ  
ZLOKALIZOWANEJ BORELIOZY Z LYME WŚRÓD PACJENTÓW  
PORADNI CHORÓB ZAKAŹNYCH W SZCZECINIE**

**Streszczenie.** Borelioza jest definiowana jako choroba zakaźna wywołana przez krętki *Borrelia burgdorferi*. Występuje w trzech fazach: wczesnej zlokalizowanej, wczesnej rozsianej i przewlekłej z możliwością zajęcia wielu narządów. W celu oceny przebiegu klinicznego, w tym przejścia w fazę zakażenia przewlekłego przeprowadzono analizę dokumentacji medycznej 175 pacjentów, którzy w 2004 roku zgłosili się do Poradni Chorób Zakaźnych w Szczecinie po leczeniu rumienia przewlekłego. Oceniano objawy kliniczne, obecność wykładników serologicznych oraz częstość przechodzenia w fazę przewlekłą zakażenia. U większości obserwowanych zakażeń ograniczyło się do rumienia wędrującego. Średni czas, w którym doszło do negatywizacji serologii w klasie IgM, wyniósł 13,2 miesiąca, 15 osób przez cały czas obserwacji wykazywało obecność przeciwciał w klasie IgM, czemu nie towarzyszyły kliniczne wykładniki choroby. U ośmiu osób (4,6%) zakażenie przeszło w formę przewlekłą – stawową. Borelioza z Lyme, o ile odpowiednio leczona w pierwszym okresie, stosunkowo rzadko przechodzi w zakażenie przewlekłe.

**Słowa kluczowe:** borelioza z Lyme, *Borrelia burgdorferi*, rumień wędrujący, przewlekła borelioza, przeciwciała przeciwboreliowe

Accepted for print – Zaakceptowano do druku: 19.07.2013

