Modern Apitherapy in the Treatment of Lyme Arthritis

Nataliia Matsko (PhD in Medical Sciences, Associate Professor, Lviv Medical University, Ukraine)
Nataliia Pokhmurska-Hudym (Family Doctor, Doctor of Alternative and Complementary Medicine, Medical Center "Pokhmursky Sisters Hospital", Ukraine)
Zoryana Ambrozevych (Doctor of Alternative and Complementary Medicine, Individual Entrepreneur Palynychak Bogdan, Ukraine)
Solomiia Tolopko (Candidate of Medical Sciences, Associate Professor, Danylo Halytsky Lviv National Medical University, Ukraine)
Mariia Ferko (Candidate of Medical Sciences, Associate Professor, Danylo Halytsky Lviv National Medical University, Ukraine)
Corresponding author: Nataliia Matsko

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Abstract. Today there is a danger of spreading Ixodes ticks, which can cause Lyme disease, which is characterized by polysystemic lesions. As a rule, treatment involves antibiotic therapy. We studied the effectiveness of apitherapy by bee sting method in the complex treatment of patients with Lyme arthritis. Patients were prescribed a course of bee stings from 1 to 15 bee stings once every other day, a total of 102 stings. After a course of apitherapy, patients had significantly reduced or eliminated pain in the spine and joints, there was a significant decrease in IgM during bee stings between courses of antibiotic therapy and IgG in tests performed after a course of treatment with bees. Apitherapy can have a pronounced antibacterial effect over the next 2 years. In addition to these findings, further observations indicated that the immunomodulatory effects of bee venom may play a crucial role in mitigating inflammatory responses. Patients not only experienced relief from pain but also reported improved mobility and overall quality of life. The gradual reduction in specific antibody levels suggests that the bee sting treatment may help recalibrate the immune system over time. This additional benefit, coupled with the direct antibacterial properties of the venom, positions apitherapy as a promising complementary treatment approach. Continued research into the long-term effects is warranted to better understand its full therapeutic potential. Moreover, the observed improvements were supported by both subjective patient reports and objective clinical measurements. The treatment appeared to modulate the inflammatory cascade associated with Lyme arthritis, leading to fewer flare-ups and a reduction in joint stiffness. This innovative method also showed potential in preventing further joint degradation, thereby extending its benefit beyond immediate pain relief. Future studies are needed to explore the optimal dosing, frequency, and possible synergies with conventional antibiotic therapies, ensuring that patients receive the most effective comprehensive care.

Keywords: Lyme disease, Lyme arthritis, bee sting, apitoxin therapy, apitoxin, Ixodes ticks.

Introduction. Today, the spread of infectious risks from ticks to human life and health is increasing. In the framework of the NorthTick project, jointly supported by the European Union through the European Regional Development Fund and the North Sea Region Programme, tick-borne disease specialists from seven North Sea countries collaborated with patient organisations and public health institutions to provide [1-3]:

- a comprehensive overview of diagnostics;
- recommendations for the treatment in the region of Lyme berylliosis, Borrelia miyamotoi infection, tick-borne encephalitis, human granulocytic infection, anaplasmosis, rickettsiosis, neoehrlichiosis and babesiosis;
- some differences in the choice and duration of antibiotic treatment, as well as in the route of administration - oral or intravenous;
- a boost for research activities on ticks.

Ticks are carriers of pathogens of viral bacterial diseases of humans and animals (Fig. 1), spreading Ixodes tick-borne borreliosis or Lyme disease [4, 5].

Fig. 1. Ticks are carriers of Lyme disease [5].

Specialists of the Ministry of Health of Ukraine have classified Lyme disease (tick-borne ixodid borreliosis) as a group of particularly dangerous infectious diseases [6]. It has been officially registered since the beginning of 2000. It was identified as a clinical manifestation in the late 1970s, after an outbreak of arthritis in children with Lyme disease in the state of Connecticut, USA [7]. Since then, the incidence of the disease has increased significantly. It tends to further increase. In 2019, 4,482 cases were registered, in 2023 - 4,911 cases of Lyme disease [8]. It is widespread in forest-steppe zones [9-11]. Untimely diagnosis leads to the appearance of chronic forms of the disease, long-term disability, the development of concomitant health disorders, disability, and fatalities [10].

According to experts from the Ministry of Health of Ukraine, the following population groups are at increased risk of Lyme disease infection: citizens living in rural areas, veterinarians, forestry workers, gas station workers and car repair workers, gas workers, tractor drivers, commanders, drivers, electricians, hunters, military personnel, forest berry and mushroom pickers, shepherds, farmers, and other categories of citizens.

According to the guidelines of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID), testing ticks for the presence of antigens or DNA of Borrelia is not recommended. Treatment of patients with Lyme borreliosis consists of specific antibiotic therapy. Most patients with Lyme arthritis are generally healthy. A slight increase in body temperature and a reaction of regional lymph nodes occur relatively often. The joint is swollen and tender, often with excessive fluid, local increase in body temperature. Swelling impairs movement. Differential diagnosis includes various types of reactive arthritis, psoriatic arthropathy, other forms of bacterial arthritis, viral arthritis, osteoarthritis, gout, pseudogout, atypical rheumatoid arthritis, sarcoidosis, trauma, etc. It is important to immediately perform all the necessary examinations for differential diagnosis. If Lyme arthritis is suspected, intra-articular corticosteroid injections should not be performed. Arthritis responds well to antimicrobial therapy: more than 90% of patients recover. Persistent Lyme arthritis, resistant to antimicrobial treatment, is rare [12, 13].

The purpose of the study was to study the effectiveness of apitherapy by bee sting in the complex treatment of patients with Lyme arthritis.

Materials and methods. Ultrasound diagnostics. The diagnostic direction – infectious lesions of the body is shown in Fig. 2.

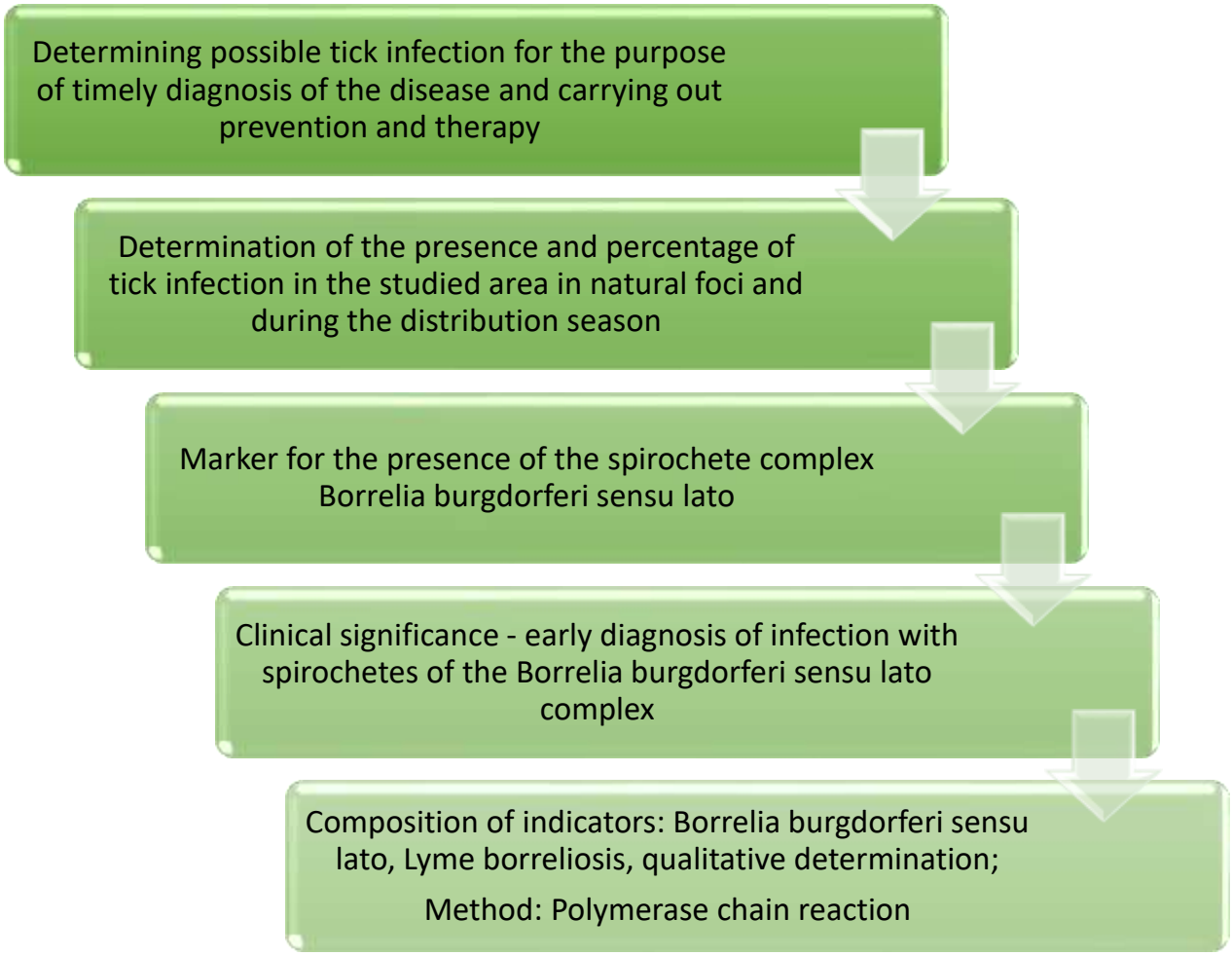


Fig. 2. Diagnostic algorithm [14].

Diagnosis is performed stepwise by enzyme-linked immunosorbent assay. In case of a positive test, confirmation by immunoblot [15].

In modern conditions, medical care for patients with Lyme disease requires interdisciplinary cooperation and integrated management of patients by a multidisciplinary team of specialists. It should involve doctors: general practitioners-family medicine, neurologists, cardiologists, rheumatologists, immunologists, infectious disease specialists, dermatologists, ophthalmologists. Registration and basic management of patients is carried out by infectious disease specialists. Doctors of various specialties should be aware of the main clinical manifestations of Lyme disease to early suspect the disease, refer patients to an infectious disease specialist for diagnostic measures and prescribe further treatment. In accordance with the order of the Ministry of Health of Ukraine dated September 21, 2024 No. 1623 "On approval of the Standard of medical care "Lyme disease"" [16] the name of the diagnosis: Lyme disease; codes of the condition or disease according to the National Classification of Diseases and Related Health Problems 025:2021 "Classifier of diseases and related health problems": A69 Other infections caused by spirochetes; A69.2 Lyme disease; Arthritis in Lyme disease (A69.2).

The study is a fragment of the scientific research work of the Lviv Medical University on the topic "Improvement of the drug circulation system during pharmacotherapy on the principles of evidence-based and forensic pharmacy, organization, technology, biopharmacy and pharmaceutical law" (state registration number 0120U105348, implementation period 2021-2026).

Results and discussion. Lyme disease (tick-borne borreliosis, Lyme borreliosis) is a naturally occurring zoonosis. It is caused by Borrelia burgdorferi sensu lato. It is transmitted to humans by transmissible transmission when an Ixodes tick bites [17-20].

Comorbidities of Lyme disease are shown in Fig. 3.

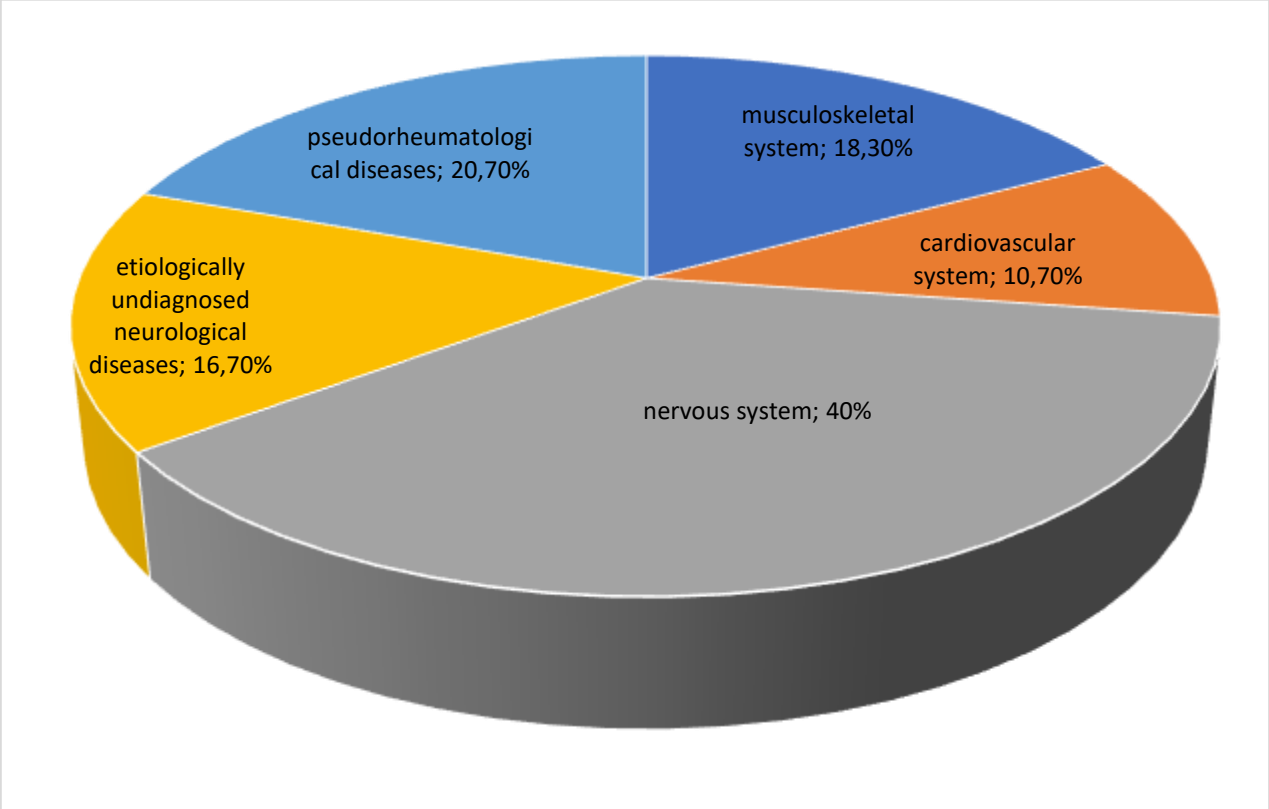


Fig. 3. Consequences of Lyme disease [17-20].

The early localized stage of Lyme borreliosis occurs 1-30 days (average 7 days) after the bite of an infected tick. The symptom of this stage of the disease is the appearance of isolated migratory erythema at the site of the pathogen, most often in the axillary, inguinal or popliteal areas. Migratory erythema is identified in 50-90% of patients with Lyme borreliosis. Usually, a papule or red spot with a seal first appears at the site of the tick bite. It is clearly delimited from healthy skin. Over time, a vesicle or pustule may form in its place (primary lesion). Gradually, the area of hyperemia expands centrifugally ("migrates"), and the center turns pale, creating the appearance of annular migratory erythema. In most cases, the diameter of the erythema is >5 cm and can reach 50 cm. Erythema migrans may be homogeneous erythematous, rather than annular. In some cases, regional lymphadenitis is noted. The general condition of patients during the early localized stage of Lyme borreliosis is usually satisfactory. Erythema migrans persists for several days-weeks. Then it disappears, leaving behind pigmentation or peeling. In 1/3 of people, the disease ends independently at this stage. In 2/3 of people, it passes to the next early disseminated stage. Characteristic is hematogenous spread of the pathogen and generalization of the infectious process. The duration of the early disseminated stage is usually 3–6 weeks. The late stage of Lyme borreliosis develops months–years after infection and is mainly characterized by the defeat of one system.

A feature of Lyme arthritis is the slow increase in symptoms from the musculoskeletal system, which may persist after a full course of treatment. Some patients develop chronic inflammatory arthritis that is resistant to antibiotic therapy. Synovitis of the knee joints is observed in the early stages of Lyme disease progression. If treatment is not carried out, 60% of patients develop Lyme arthritis. Joint damage in Lyme arthritis is caused by hematogenous spread of the borreliosis pathogen and its entry into the joint tissue in the first days of the disease. During this period, the specific immune response to Borrelia is minimal. Joint damage can be in the form of recurrent arthritis. It lasts up to 5 years. Bursitis, enthesopathy, ligamentitis are characteristic of chronic arthritis. In later stages

of development, signs of inflammatory (osteoporosis, cartilage loss) and degenerative (meniscal ossification, osteophytes, cysts, subchondral sclerosis) processes are observed [21].

Clinical signs of Lyme arthritis are shown in Fig. 4.

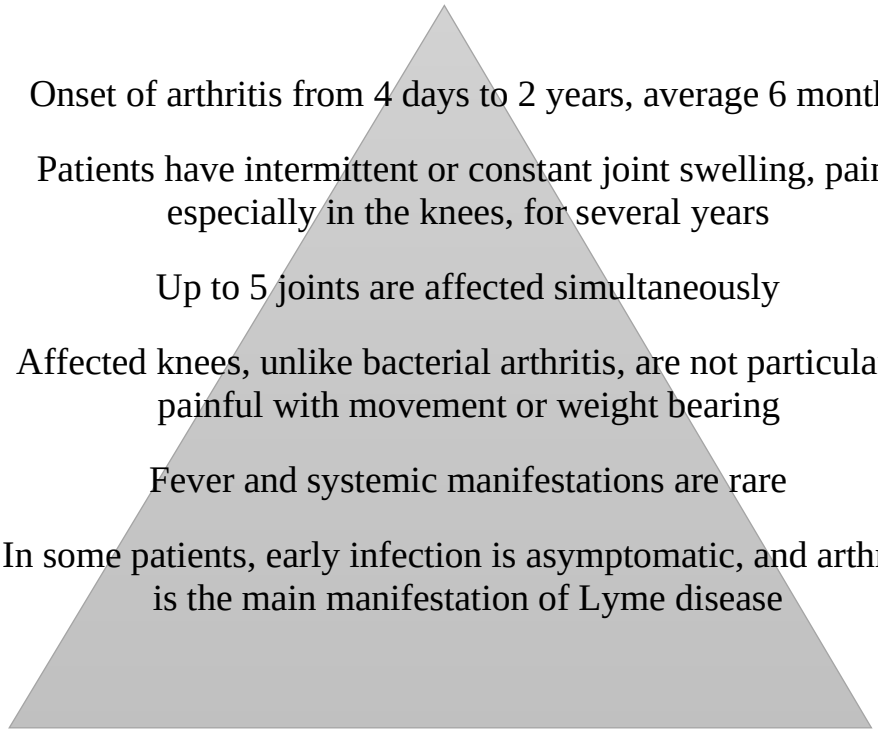


Fig. 4. Clinical features of Lyme arthritis [21].

The clinical features of Lyme disease are shown in Fig. 5.

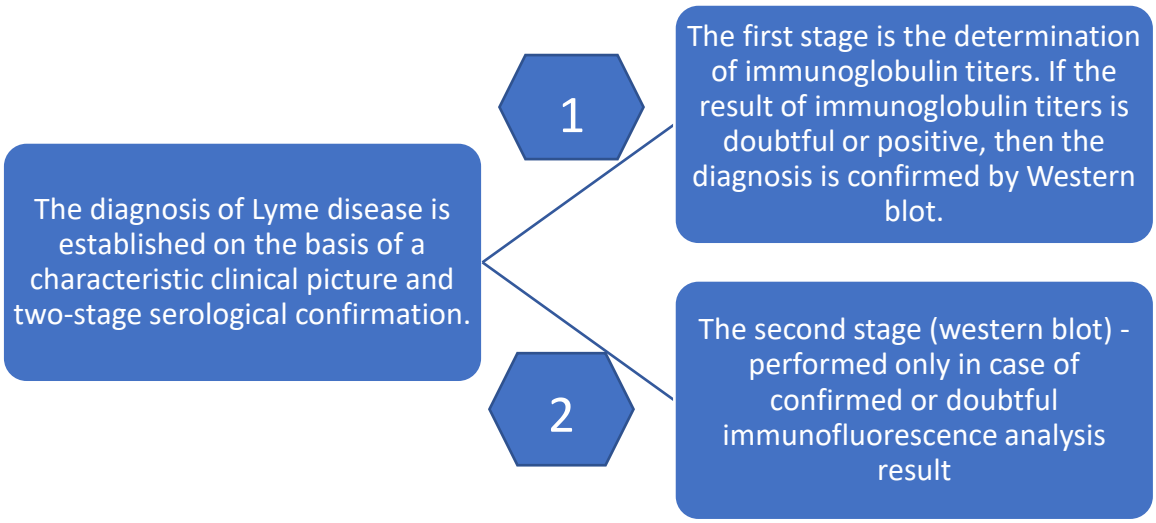


Fig. 5. Clinical signs of Lyme disease [21].

Western blot is a highly sensitive and highly specific diagnostic technique aimed at determining immunoglobulins to specific Borrelia antigens. In case of detection of positive IgM and negative IgG, it is necessary to perform a repeated Western blot after 2 weeks.

Analysis of the current situation in Ukraine shows that the largest number of patients with Lyme borreliosis is recorded in Kyiv and Lviv region. In total, 252 cases were recorded in Lviv region

in 2023, which is 9.8% fewer patient visits (278) compared to 2022. The intensive rate per 100 thousand population also decreased from 11.09 in 2022 to 10.05 in 2023. The decrease in the intensity of the indicators may indicate that the number of citizens who have been bitten by ticks is latent or they were self-medicated or had a mild form of the disease. According to forecasts, the number of patients with Lyme borreliosis in 2023 may be 5-7 times higher. Cases of Lyme disease were registered in all districts of the Lviv region [22, 23], which is shown in Fig. 6.

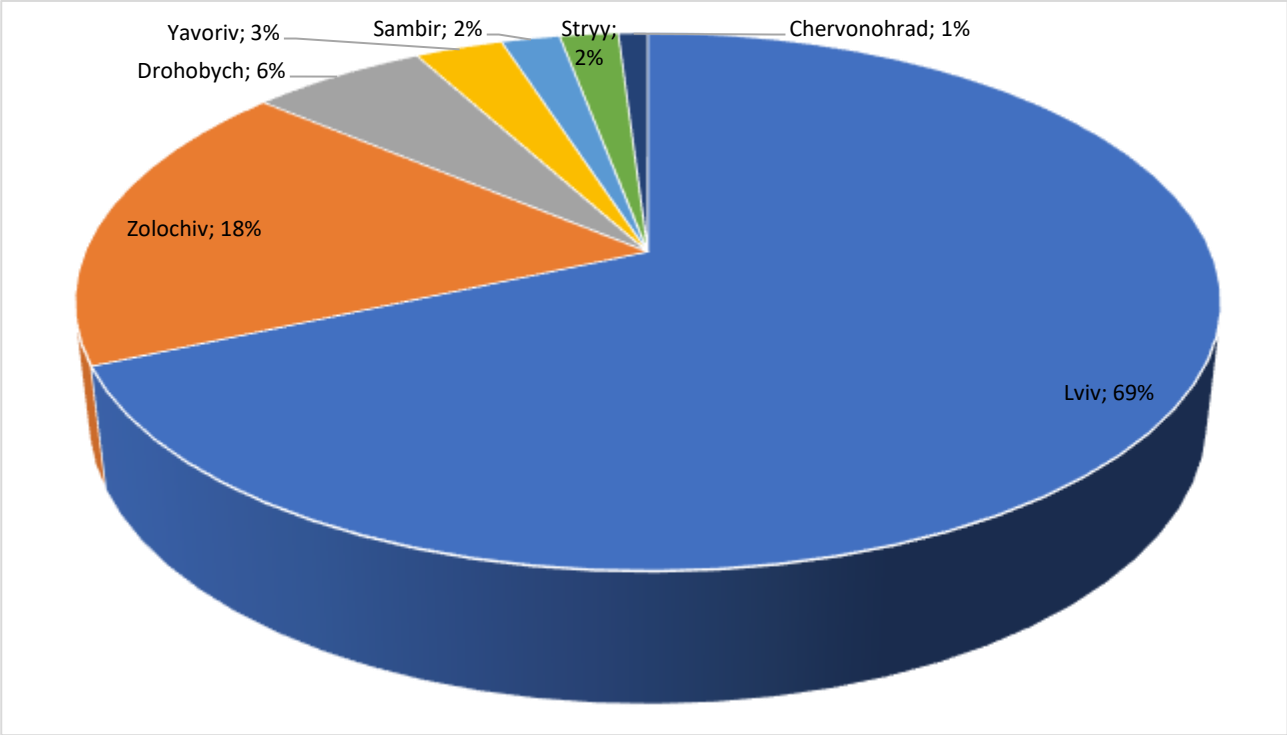


Fig. 6. Dynamics of the distribution of Lyme disease cases in the districts of Lviv region in 2023 [22, 23].

To provide medical care to the population in Lviv region, 58 citizen patients with complaints of the musculoskeletal system applied to the medical center "Pokhmursky Sisters Hospital" [24] in the period from 2022 to 2024. It is illustrated (Fig. 7) that at the site of a tick bite, a papule or a red spot with a seal first appears, which is clearly delimited from healthy skin [25].

During the study, patients were divided into two groups:

- The first group – 40 patients who had a confirmed diagnosis of Lyme arthritis and who received a course of antibiotic therapy, but complaints from the musculoskeletal system remained.
- The second group – 18 patients who had various complaints from the musculoskeletal system. The patients were recommended to determine the titers of immunoglobulins to Borrelia burgdorfer sensu lato. The test results were positive. Alternative medicine doctors referred them to infectious disease doctors for a consultation. A course of antibiotic therapy was prescribed. The work was coordinated with the participation of family doctors.

At the same time, the patients were prescribed a course of bee stings from 1 to 15 bee stings once every other day. A total of 102 stings. For patients who had an allergic reaction to bee stings, the number of stings at a time was limited from 1 to 5. At the same time, antihistamines were prescribed. The number of bee stings per course was also 102 bee stings, but for a longer period of days used. For the prevention of Lyme disease, two vaccines were developed in 1990 – LYMErix (SmithKline Beecham) and ImuLyme (Pasteur Merieux Connaught) [26]. The immunogenetic protein OspA (outer surface protein A) was used as the antigen. The LYMErix vaccine was licensed in the USA on December 21, 1998.

Fig. 7. Picture at the site of a tick bite [25].

During a detailed interview with doctors, it was found that all patients who applied to the Pokhmursky Sisters Hospital complained of:

- general fatigue;
- headache;
- muscle soreness and tension;
- swelling and pain in the affected joints;
- in patients of the first group, damage was observed mainly in one joint (55%), in patients of the second group - in two or more joints (72%);
- regarding localization, the inflammatory process in patients of the first group was more often observed in the knee joints (72%), hip (18%), and elbow (10%). Patients of the second group suffered from damage to the knee and hip joints (85%), and knee and elbow (10%). The radiocarpal and ankle joints were rarely affected.

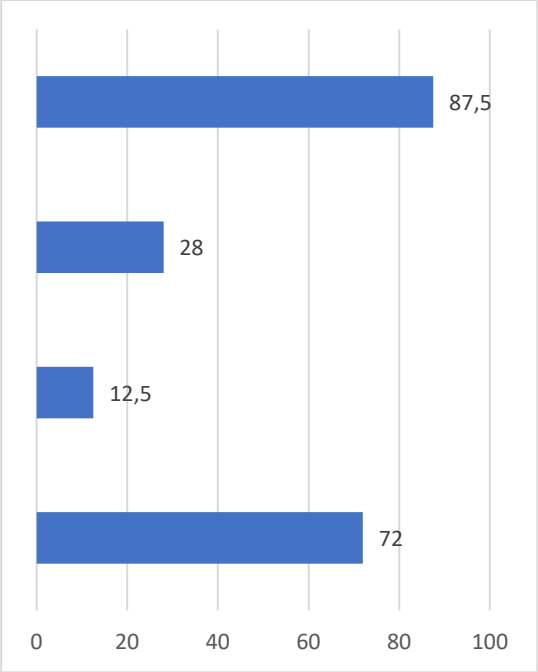
On ultrasound diagnostics of large joints in patients of the first group, swelling of the articular surfaces, signs of tendovaginitis, tendonitis were noted. Patients in the second group had arthritis, moderate synovitis, tendonitis, tendosynovitis, bursitis, enthesopathy, fibrositis of the intra-articular ligaments and menisci of the knee joints, manifestations of degenerative changes in the articular

surfaces of the femur and tibia, edema of paraarticular tissues. The motor activity of patients in the second group was reduced due to edema and soreness of the joints.

In all patients in the first group, despite antibiotic therapy, an increase in IgM and IgG antibodies was observed. Patients were referred for a second consultation with an infectious disease specialist. After a course of apitherapy, patients had significantly reduced (13 people) or completely resolved (45 people) pain in the spine and joints. Their edema decreased, mobility improved, and the constant feeling of cold in the joints significantly decreased. Ultrasound diagnostics noted the disappearance of signs of synovitis and tendosynovitis.

In patients of the second group (8 people) after the course of antibiotic therapy, a temporary decrease in IgM and IgG antibodies was noted. This can be explained by the resistance of this strain of Borrelia burgdorferi sensu lato to drugs. The authors of the article noted a decrease in IgM during bee stings between courses of antibiotic therapy and IgG in the analyzes that were performed after the course of treatment with bees. At this time, the patients no longer took antibiotics, and the break between treatment with apitherapy and antibiotics in these patients was 1 month.

The authors of the article indicate a pronounced antibacterial effect of apitoxin and apitherapy over the next 2 years. (Fig. 8).



- 35 (87.5%) patients of the first group were not bothered by symptoms associated with inflammatory processes in the joints and did not apply for a repeated course of apitherapy.
- 5 (12.5%%) patients experienced joint pain only in the cold season, but of much lower intensity. They applied again after 6-12 months.
- 5 (28%) patients of the second group did not apply for repeated treatment due to the absence of symptoms of the disease.
- 13 (72%) patients applied again for a course of apitherapy after 3-12 months, more often in the cold season. Also, these patients underwent 1-2 repeated courses of antibiotic therapy in the interval between courses of apitherapy.

Fig. 8. Characteristics of the antibacterial effect of apitoxin and apitherapy during the next 2 years in patients of the first and second groups.

All patients noted a noticeable decrease in pain and improvement in motor activity, both immediately after the course of apitherapy and for several months after it. Such results suggest that in complex treatment with antibiotic therapy, bee stings can enhance its effectiveness.

It should be noted that the website of the Ministry of Health of Ukraine published a publication entitled “Caution! Unproven rehabilitation: apitherapy” [27]. It is noted that high-quality and effective rehabilitation is fully covered by the National Health Service of Ukraine within the framework of the Medical Guarantees Program. At the same time, the publication emphasizes that:

- ✓ in the USA there is still an association of apitherapists, which is actively testing various methods of treatment with bees;
- ✓ the so-called apitherapy – a direction of alternative medicine that uses beekeeping products, in particular, honey, pollen, propolis, royal jelly and bee venom;
- ✓ some doctors believe that there is a high probability of side effects [28].

It is noteworthy that in Ukraine, leading scientists of European and world level Tykhonov O.I., Tykhonova S.O., Shapovalova V.O., Yarnykh T.G., Shpychak O.S., Osyntseva A.O., Georgievsky V.P., Zbrozhek S.I., Pastalitsya S.V., Gudzenko A.O., Vasina Yu.V., Shapovalov V.V., Budnikova T.M., Pashnev P.D., Yegorov I.A., Demyanenko V.G., Syatyna M.L., Kurchenko I.N., Tsyshnetskaya A.V., Nevzgoda O.A., Voloshyna N.P. and others. on the principles of evidence-based pharmacy and evidence-based medicine, multidisciplinary research is conducted. The feasibility of the apitherapeutic direction is substantiated. Scientific, theoretical, and practical development of combined medicines based on beekeeping products is proposed. Dosage forms based on beekeeping products have been developed: aerosols, tablets, capsules, injection solutions, eye drops, ointments, creams, gels, syrups, extracts. The results [29-72] have been implemented in industrial production and medical practice in accordance with the ICD-11:

- biopharmaceutical studies on the completeness and rate of release of biologically active compounds from beekeeping products;
- physicochemical, structural-mechanical, osmotic studies on the substantiation of the method and procedure for the introduction of active and auxiliary substances;
- the influence of filter materials on their quality indicators, based on which the optimal materials of 9 filter membranes were proposed for the industry.

Bee venom (apitoxin) is a poison of biological origin [73, 74]. The bee (Fig. 9) produces apitoxin:

- ✓ special organs of worker bees and queens;
- ✓ drones have neither poisonous glands nor stings;
- ✓ in worker bees, the sting is an organ of active protection of the bee colony from enemies, and in the queen, it performs a dual function - it is used for laying eggs and for a deadly battle with a rival that appears in the colony;
- ✓ the poison is secreted by two poisonous glands located in the last segments of the abdomen of worker bees;
- ✓ the large venom gland consists of a long-branched tube in which the venom is produced and a pear-shaped reservoir where it is stored;
- ✓ the secretion of the large venom gland has an acidic reaction; therefore, this gland is also called “acidic”;
- ✓ the small venom gland is a short tube located at the base of the organ along which the sting moves and secretes a secretion that has an alkaline reaction;
- ✓ the chemical composition of the venom of both glands is complex, i.e.:
- ✓ the main part of the venom is secreted by the large gland and the pH depends on its acidic environment;
- ✓ properties of bee venom: cause pain; swelling; redness at the site of the sting.

The chemical composition of bee venom is characterized by the following components [75-79]:

- is a syrupy yellowish liquid with an aroma resembling the smell of honey;
- has a bitter taste and an acidic reaction (pH = 4.5–5.5);
- the dry matter content ranges from 30 to 45%;
- dried bee venom is a multicomponent mixture of organic and inorganic substances;
- more than 50 different substances and ash elements have been identified;
- the ash content of bee venom is 3-4% of the dried venom;
- phosphorus, calcium, magnesium, copper have been identified in the ash. Chlorides are present in minimal quantities. Among the low-molecular organic compounds are biogenic amines: histamine (0.34 – 0.5%), dopamine and noradrenaline;
- fat-like substances are contained in low concentrations: 1–3%;
- free amino acids are contained about 1%;
- the main part of the dry matter (80%) is proteins and peptides, they are active biochemical and pharmacological components of bee venom.

Fig. 9. Bee [73].

Melittin (Fig. 10) is isolated from bee venom. It makes up 50–55% of the dry venom. Melittin is a peptide consisting of 26 amino acids. It was named after the bee – melittin [80].

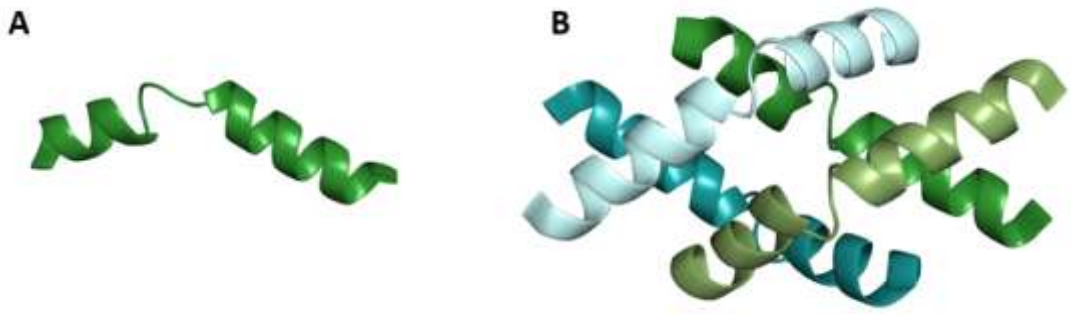


Fig. 10. Three-dimensional structure of melittin. (A) The helical monomer consists of two helical segments. (B) Tetrameric assembly of melittin [80].

Established that the amino acids in the melittin molecule are in a special order: alkaline hydrophilic amino acids are located at one end (C-terminus), and hydrophobic ones at the other end (X-terminus) of melittin. It is this arrangement of amino acids that is the structural basis of the property of melittin to reduce the surface tension of solutions. This ability makes it possible to destroy not only blood cells, but also other cells and their organelles. Melittin penetrates the cell membrane of leukocytes and destroys lysosomes and mitochondria. Cytolysis of some leukocytes causes the appearance of biogenic amines – histamine and serotonin, which significantly enhances the inflammatory reaction. It has been established that under the influence of melittin, the biosynthesis

of prostaglandins, anti-inflammatory substances with a hormone-like effect, is enhanced. Melittin disrupts the blood clotting process and oxidative phosphorylation in mitochondria. It is known that bee venom stimulates the activity of the pituitary-adrenal system. Melittin suppresses the immune response. The radioprotective effect of bee venom was confirmed by scientists from the USA and Japan [80].

The pharmacological properties of melittin are shown in Fig. 11.

lowering blood pressure	anti-inflammatory action	vasodilator action
preventing atherosclerosis	therapeutic doses increase tone	anticoagulant action
antibacterial effect	inhibits the growth of gram-positive bacteria	antirheumatic properties

Fig. 11. Pharmacological properties of melittin [80].

Bee venom contains apamin, a peptide that stimulates the central nervous system. The peptide consists of 18 amino acids. The anti-inflammatory effect of apamin is 1000 times greater than that of some non-steroidal anti-inflammatory drugs. Apamin has almost no antigenic and allergic properties.

Bee venom contains the peptide Mast Cell Degranulating. The name Mast Cell Degranulating is given to the peptide for its ability to dissolve mast cell granules. The peptide consists of 22 amino acids. Its alkaline properties depend on the presence of 9 alkaline amino acids. It has a powerful anti-inflammatory effect.

Adolapine is found in bee venom. It has two biologically active components that have a powerful analgesic effect. The polypeptide chain consists of 103 amino acids. It inhibits the activity of two key enzymes of the metabolic processes of inflammation biosynthesis – cyclooxygenase and lipoxygenase. The analgesic effect is due to its property to slow down the biosynthesis and pharmacological activity of prostaglandins E, which reduce the pain threshold.

Bee venom hyaluronidase belongs to the group of enzymes. It is involved in the breakdown of hyaluronic acid and other complex polysaccharides. These compounds are part of the intercellular fluid of connective tissue and membranes. Their breakdown increases the permeability of cells and tissues. Bee venom hyaluronidase is the most active enzyme of mucopolysaccharides. The highest activity of the drug is manifested in an environment with pH=4-5. The enzyme is thermolabile – it loses its activity when heated. It is believed that the amount of hyaluronidase in bee venom is 2-3%. The biological role of hyaluronidase in bee venom is to facilitate the penetration of venom into the tissues of another organism with its subsequent resorption [80].

Phospholipase, as a factor that enhances the hemolytic activity of bee venom after the addition of lecithin. In the phospholipid molecule, bee venom phospholipase cleaves a fatty acid. Phospholipase is the most stable of all bee venom enzymes. The pharmacological and toxic properties of phospholipase are due to its biological activity. Phospholipase reduces blood clotting, damages mitochondrial membranes. Of all the components of bee venom, phospholipase is the strongest antigenic and allergenic irritant [80].

Alpha-glucosidase – the amount of this enzyme in the venom is less than 1%. It is an antigen and has allergic properties. Lysophospholipase belongs to glycoproteins. The greatest activity of this enzyme is manifested at pH 9.0. The biological action of bee venom lysophospholipase is defined as antitoxic. There is an assumption that it can be an antigen and allergen of bee venom. It is believed that 300-400 bee stings in a person with a normal reaction to bee venom can be lethal [80].

Antiserum against bee venom has been obtained from immunized horses. Allergic reactions caused by bee venom are considered anaphylactic. Literature data recommend that allergy sufferers who are severely tolerant to bee stings undergo a course of desensitizing treatment.

Bee venom contains components that have various anti-inflammatory properties. A significant advantage of the peptide components of bee venom over nonsteroidal anti-inflammatory drugs is that the former exhibit their pharmacological action in very small doses and their therapeutic index is hundreds of times greater. Bee venom has been used in folk medicine since ancient times. Evidence

of the healing properties of bee venom is found in the works of ancient physicians Hippocrates (2nd–3rd centuries BC), Pliny (1st century), and Galen (2nd century). In the 19th century, treatment with bee venom was widespread mainly in Europe. From 1888 to 1912, articles by the Czech doctor F. Terch on the treatment of many patients with bee stings were published in Viennese journals.

Doctors of various specialties should be aware of the main clinical manifestations of Lyme disease [81-88]:

- ✓ the diagnosis may be suspected at different stages of the course, depending on this, the patient will need to use different examination methods;
- ✓ patients with Lyme disease may have lesions of the skin, nervous and cardiovascular systems, musculoskeletal system, and eyes;
- ✓ multisystem lesions complicate clinical diagnosis, for which Lyme disease has been called the "great imitator" of various human diseases;
- ✓ complete clinical examination (neurological, cardiological, rheumatological, ophthalmological, and dermatological) is performed according to indications for each patient with positive serological tests for Lyme disease;
- ✓ medical and pharmaceutical care for patients with Lyme disease requires interdisciplinary cooperation and integrated management of patients by a multidisciplinary team of specialists, which should include doctors: general practitioners-family medicine, neurologists, cardiologists, rheumatologists, immunologists, infectious disease specialists, dermatologists, ophthalmologists, pharmacists, and other specialists.

Conclusions. Doctors of various specialties should be aware of the main clinical manifestations of Lyme disease to early suspect the disease, refer patients to an infectious disease specialist for diagnostic measures and prescribe further treatment. The diagnosis may be suspected at different stages of the course, depending on this, the patient will need to use different examination methods. Patients with Lyme disease may have lesions of the skin, nervous and cardiovascular systems, musculoskeletal system, and eyes. Multisystemic lesions complicate clinical diagnosis, for which Lyme disease has been called the "great imitator" of various human diseases. A complete clinical examination (neurological, cardiological, rheumatological, ophthalmological and dermatological) is performed as indicated for each patient with positive serological tests for Lyme disease. Medical care for patients with Lyme disease requires interdisciplinary cooperation and integrated management of patients by a multidisciplinary team of specialists, which should include doctors: general practitioners-family medicine, neurologists, cardiologists, rheumatologists, immunologists, infectious disease specialists, dermatologists, ophthalmologists, and other specialists; registration and basic management of patients is carried out by infectious disease doctors. Modern apitherapy is effective for the treatment of pain in patients with Lyme arthritis. The authors' data indicate that the decrease in antibodies to Borrelia burgdorfer between courses of antibiotic therapy reliably indicates the etiotropic effect of apitoxin on the pathogen itself. Given the significant spread of Lyme disease borreliosis, it is advisable to suspect the borreliosis nature of the disease in the case of treatment-resistant neuritis, radiculitis, encephalitis of unknown etiology and to recommend apitherapy to such patients in complex treatment, especially during the acute stage of the disease. To obtain positive results, the apitherapist should work in compliance with an infectious disease specialist, immunologist, cardiologist, neurologist, family doctor, pharmacist and combine treatment with bee stings with unified clinical protocols for the treatment of Lyme disease. Apitherapy for Lyme disease, on a professional basis, should be practiced by alternative medicine doctors who have undergone specialization and have knowledge and skills in the use of bee venom. Further research is needed to develop pharmacoeconomic calculations of apitherapy and the use of bee venom in the pharmacotherapy of a wide range of diseases.

Declaration of conflict interest. The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. The authors confirm that they are the authors of this work and have approved it for publication. The authors also certify that the obtained clinical data and research were conducted in compliance with the requirements of moral and

ethical principles based on medical and pharmaceutical law, and in the absence of any commercial or financial relationships that could be interpreted as potential conflict of interest.

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Ethical approval. Ethical clearance was obtained from the administration of the Lviv Medical University. Permission statement for conducting the experiments was received from the administration of the Lviv Medical University. Before any data collection, the main purpose of the study was clearly explained to each department (concerned personnel).

Data availability statement. The datasets analyzed during the current study are available from the corresponding author on reasonable request.

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