Lyme Disease

A Comprehensive Public Health Review

Layered for the public, clinicians, and scientists

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Tick-borne disease • Borrelia burgdorferi • Prevention, diagnosis & treatment

Evidence assembled with SourceTracer™ · Figures generated with FigureLabs / SourceTracer™

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Disclaimer

This article has not been peer-reviewed. Readers who identify any inaccuracies are encouraged to contact the author, who will review and make appropriate corrections.

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How to read this review

This review is built in three layers so that one document can serve very different readers. Within each topic you will find the same material presented at three depths, marked by a colored tag. You can read straight through, or follow only the layer that matches your needs.

At a glance — for general readers gives a plain-language explanation with no jargon.

Clinical detail — for physicians adds the practical decision-making, dosing, and diagnostic nuance a clinician needs at the bedside.

Mechanistic depth — for scientists covers molecular biology, immunology, vector ecology, and open research questions.

Summary

Lyme disease (Lyme borreliosis) is the most common vector-borne disease in the United States and the temperate Northern Hemisphere. [1,2,3] It is caused by spirochaetal bacteria of the *Borrelia burgdorferi* sensu lato complex, transmitted to humans by the bite of *Ixodes* ticks. [3,5] In the United States, surveillance records tens of thousands of cases annually, but modeling of insurance and laboratory data suggests roughly 476,000 people are diagnosed and treated each year. [7] Most infections begin with the expanding skin lesion erythema migrans and are cured with a short course of oral antibiotics; untreated infection can disseminate to the nervous system, heart, and joints. [3,4] Diagnosis outside of the classic rash relies on standardized two-tier serology. [14] A minority of patients report persistent symptoms after treatment (post-treatment Lyme disease syndrome), for which prolonged antibiotics have not shown benefit. [20,21] Prevention rests on tick-bite avoidance, with vaccines again in advanced development. [4,20]

1. Introduction and historical background

At a glance — for general readers

Lyme disease is an illness you can catch from the bite of a tiny tick. It is named after Lyme, Connecticut, where in the 1970s an unusual cluster of children developed swollen, painful joints. Investigators eventually traced the illness to bacteria carried by ticks. [2,3] Today it is the most commonly reported tick-borne illness in the country. [1,28] The good news is that when it is caught early, it is almost always curable with antibiotics. [3,27]

Clinical detail — for physicians

Lyme disease was characterized as a distinct clinical entity following the 1975 investigation of juvenile arthritis in Lyme and Old Lyme, Connecticut; the spirochaetal cause, *Borrelia burgdorferi*, was identified by Willy Burgdorfer in 1981–82. [2,3] Clinicians should understand the disease as a staged, multi-system infection in which the probability of each manifestation depends on the duration of untreated infection and on the geographic genospecies. [3,4]

Mechanistic depth — for scientists

The *B. burgdorferi* sensu lato complex now comprises more than 20 named genospecies. In North America, human disease is overwhelmingly caused by *B. burgdorferi* sensu stricto, whereas in Eurasia *B. afzelii* and *B. garinii* predominate and shape distinct clinical phenotypes (e.g., acrodermatitis chronica atrophicans with *B. afzelii*).[3] The organism is a fastidious, microaerophilic spirochaete with an unusual segmented genome (a linear chromosome plus numerous linear and circular plasmids) that encodes the surface-lipoprotein machinery underpinning host adaptation and immune evasion.[5,9]

2. The pathogen, the tick, and the enzootic cycle

At a glance — for general readers

The bacteria live in a natural cycle between ticks and small animals such as mice and other rodents; deer are important for feeding adult ticks (Figure 1). Humans are accidental hosts who get bitten when they spend time in grassy or wooded areas.[5,6] The ticks that spread Lyme disease are very small — the young 'nymph' stage is about the size of a poppy seed — which is why bites are so easily missed (Figure 2).[1]

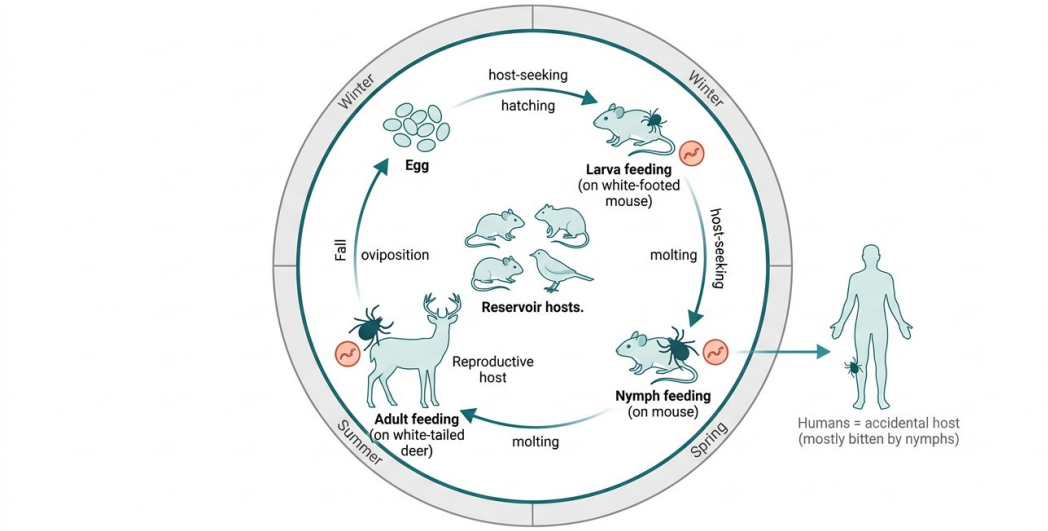

Figure 1. The enzootic cycle of Borrelia burgdorferi

Borrelia is maintained in a roughly two-year cycle: larvae and nymphs feed on reservoir hosts such as the white-footed mouse, while adults feed and mate on white-tailed deer. Humans are accidental hosts, most often bitten by nymphs in spring and summer.

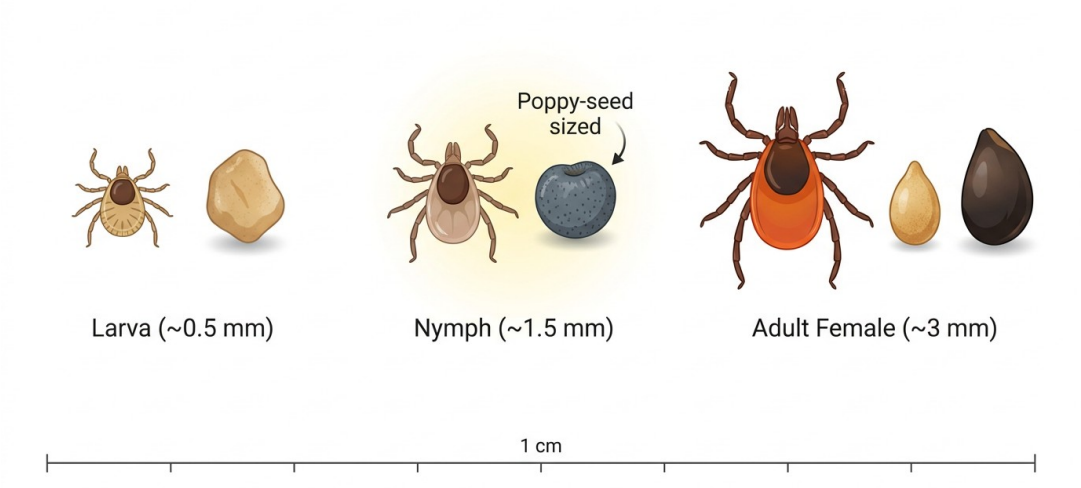

Figure 2. Ixodes tick life stages shown at actual size

The larva, nymph, and adult female of the blacklegged tick (Ixodes scapularis) at true relative size, beside everyday objects for scale. The poppy-seed-sized nymph causes most human infections and is easily overlooked.

Clinical detail — for physicians

In the eastern and upper-midwestern US the vector is *Ixodes scapularis* (the blacklegged or deer tick); on the Pacific coast it is *I. pacificus*; in Europe, *I. ricinus*. [3,5] Transmission risk rises sharply after the tick has been attached and feeding for 36–48 hours, which is the rationale for prompt tick removal and for time-limited post-exposure prophylaxis. [4,8] Nymphs feeding in late spring and early summer cause most human infection because they are abundant, infectious, and inconspicuous. [1]

Mechanistic depth — for scientists

The spirochaete persists across a two-year enzootic cycle by reprogramming its transcriptome at each transition between the arthropod and vertebrate niches. Outer surface protein A (OspA) mediates colonization of the tick midgut, while a reciprocal switch to OspC is required for migration to the salivary glands and transmission to the mammalian host during the bloodmeal (Figure 3). [5,6] Tick salivary proteins (e.g., Salp15) and modulation of the vector microbiome and immune pathways (JAK–STAT, IMD) facilitate spirochaete survival and host infection; the bacterium even induces metabolic reprogramming (glycolysis) in tick cells. [5] Antigenic variation of the VlsE lipoprotein, complement-regulator acquisition, and downregulation of immunogenic surface proteins together allow immune evasion and dissemination. [9]

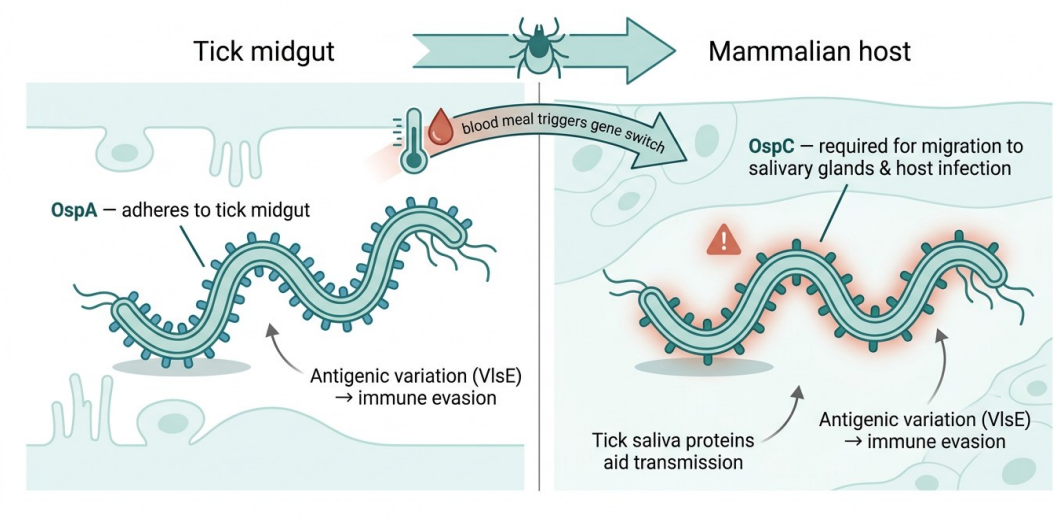

Figure 3. The OspA-to-OspC molecular switch across the tick–host transition

In the tick midgut the spirochaete expresses OspA; the blood meal triggers a switch to OspC required for migration to the salivary glands and infection of the mammalian host. Antigenic variation (VlsE) and tick salivary proteins support immune evasion and transmission.

Table 1. Principal Ixodes vectors and Borrelia genospecies by region

Region	Primary tick vector	Dominant genospecies	Hallmark late feature
Northeastern & upper-midwestern US	*Ixodes scapularis*	*B. burgdorferi* s.s.	Lyme arthritis
Pacific coast US	*Ixodes pacificus*	*B. burgdorferi* s.s.	Lyme arthritis
Europe	*Ixodes ricinus*	*B. afzelii*, *B. garinii*	Acrodermatitis chronica atrophicans; neuroborreliosis
Asia	*Ixodes persulcatus*	*B. garinii*, *B. afzelii*	Neuroborreliosis

Sources: *Steere et al. 2016; Kurokawa et al. 2020; Lantos et al. 2021.*

3. Epidemiology and the public-health burden

At a glance — for general readers

Lyme disease is common and getting more so. Although about 30,000–60,000 cases are formally reported each year, the true number of Americans diagnosed and treated is far higher — close to half a million per year.[1,7] Most cases happen in the Northeast, mid-Atlantic, and upper Midwest, and most people are infected close to home, in their own yards and neighborhoods (Figure 4).[1] Lyme disease is also climbing quickly in Canada — especially in Ontario, Quebec, and the Maritime provinces — as the ticks that carry it push northward.[38]

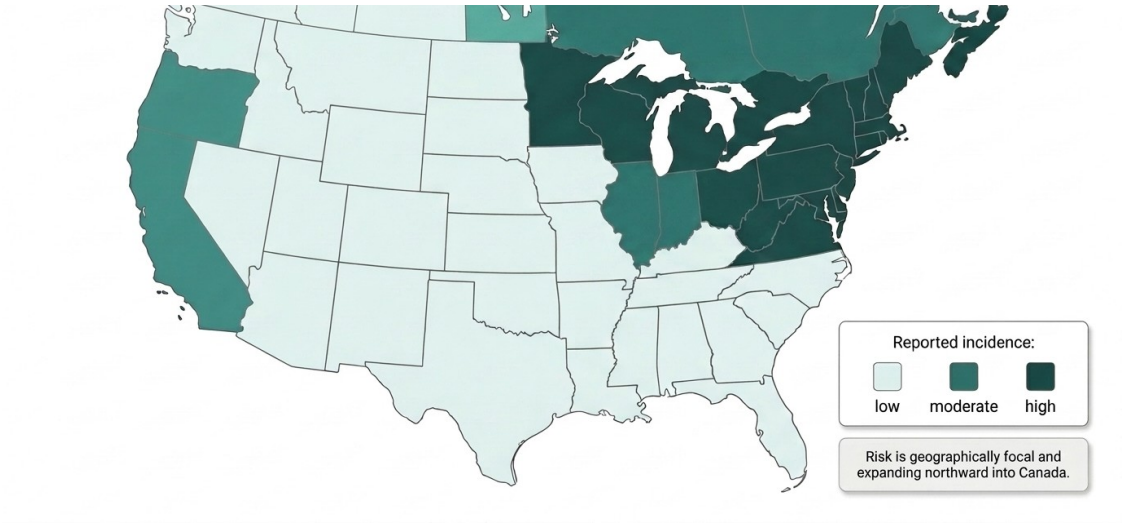

Figure 4. Where Lyme disease risk is highest in North America

Reported incidence is geographically focal: risk concentrates in the US Northeast, mid-Atlantic, and upper Midwest, with moderate risk on the upper West Coast. Endemic risk now also extends into eastern and central Canada — southern Ontario, southern Quebec, and the Maritimes — and is expanding northward. Most exposure occurs close to home.

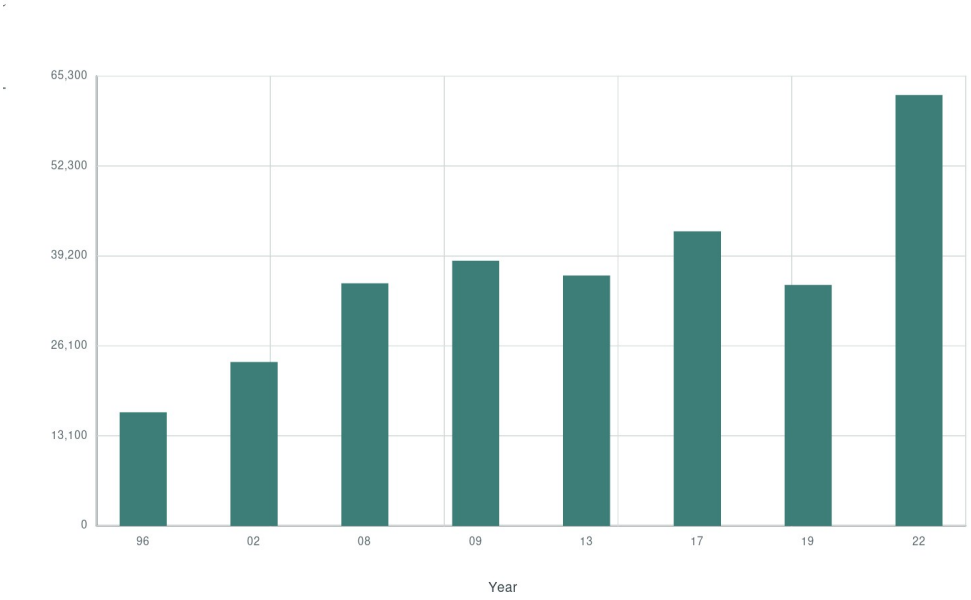

Figure 5. Reported Lyme disease cases in the United States, 1996–2022

CDC national surveillance counts (selected years). The 2022 increase partly reflects a revised surveillance case definition adopted in January 2022, not solely a true rise in incidence. Values illustrate established CDC reporting patterns.

Clinical detail — for physicians

Reported incidence is highly focal: a small number of high-incidence states account for the great majority of cases. [1] Two epidemiological features are clinically useful. First, incidence is bimodal by age, peaking in children aged roughly 5–15 years and again in adults over 50 (Figure 6). [1,22] Second, onset is strongly seasonal, clustering in June and July in step with nymphal questing (Figure 7); a diagnosis of early Lyme disease in mid-winter in a non-endemic area should prompt scrutiny. [1] Pre-test probability — driven by season, geography, and exposure — should govern testing and empiric treatment decisions.

[4,8] The same seasonality and bimodal age pattern hold in Canada, where reported cases rose roughly eighteenfold — from 144 in 2009 to 2,634 in 2019 — and remain concentrated in Ontario, Quebec, and Nova Scotia (about 92% of cases); clinicians in newly endemic Canadian regions should apply the same exposure-based reasoning. [38]

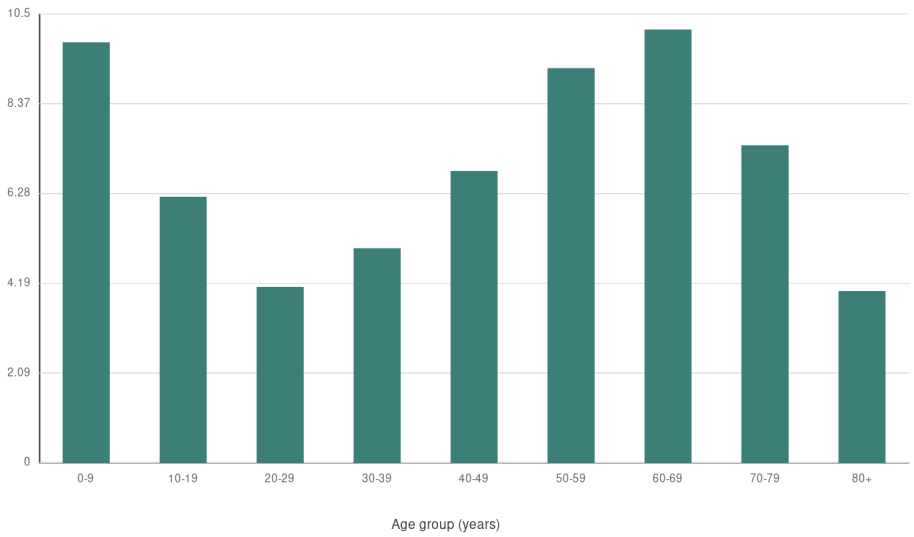

Figure 6. Bimodal age distribution of Lyme disease incidence

Incidence peaks among children aged 5–14 years and adults aged 50–69 years — a pattern consistent across US surveillance. Values are representative.

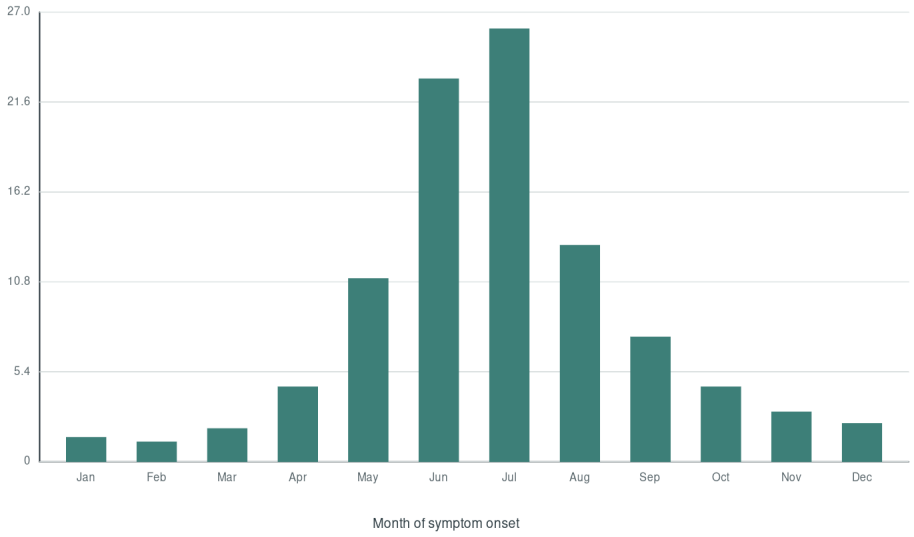

Figure 7. Seasonal onset of Lyme disease by month

Onset peaks sharply in June–July, coinciding with the questing activity of nymphal Ixodes ticks and increased human outdoor exposure. Values are representative of CDC surveillance patterns.

Mechanistic depth — for scientists

Surveillance counts substantially understate true incidence; analyses of commercial-insurance claims and laboratory testing volumes converge on an estimate of approximately 476,000 diagnosed-and-treated cases annually in the US. [7] Other US epidemiologic reviews similarly emphasize that passive surveillance substantially undercounts true incidence. [36] Interpreting trends requires care: the apparent jump in 2022 reflects, in large part, a deliberately simplified surveillance case definition for high-incidence jurisdictions rather than a true epidemiologic surge. [2] Drivers of long-term expansion include reforestation, suburban encroachment into tick habitat, growth of deer populations, and climate-mediated changes in tick range and phenology. [2,25,26] Canada is a clear sentinel of this expansion: temperature-driven population models project, and surveillance confirms, the northward establishment of *Ixodes scapularis* across eastern and central Canada through the coming decades, with corresponding emergence of human Lyme disease. [39,40]

4. Clinical manifestations and natural history

At a glance — for general readers

The earliest and most common sign is a gradually expanding circular rash at the bite site, often (but not always) clearing in the center so it looks like a 'bull's-eye.' This is called erythema migrans (Figure 10). [10] People may also feel flu-like — tired, achy, feverish. If the infection is not treated, weeks to months later it can spread and affect the nerves (for example causing a drooping face), the heart, or the joints (especially a swollen knee). [3,11,12,13]

Clinical detail — for physicians

Lyme disease is classically staged as early localized, early disseminated, and late disease, though manifestations overlap (Figure 9). [3] Erythema migrans (EM) is present in roughly 70–80% of recognized cases and is a clinical diagnosis — serology is unnecessary and often negative this early (Figure 8). [10,14] Early disseminated disease includes multiple EM lesions, cranial neuropathy (notably unilateral or bilateral facial palsy), lymphocytic meningitis, radiculopathy, and carditis with variable atrioventricular (AV) block. [11,12] Lyme carditis, though rare (~1% of cases), can cause high-grade AV block and warrants telemetry; it is usually reversible with therapy. [12] Late disease in North America is dominated by Lyme arthritis — intermittent or persistent monoarticular or oligoarticular swelling, classically of the knee. [13]

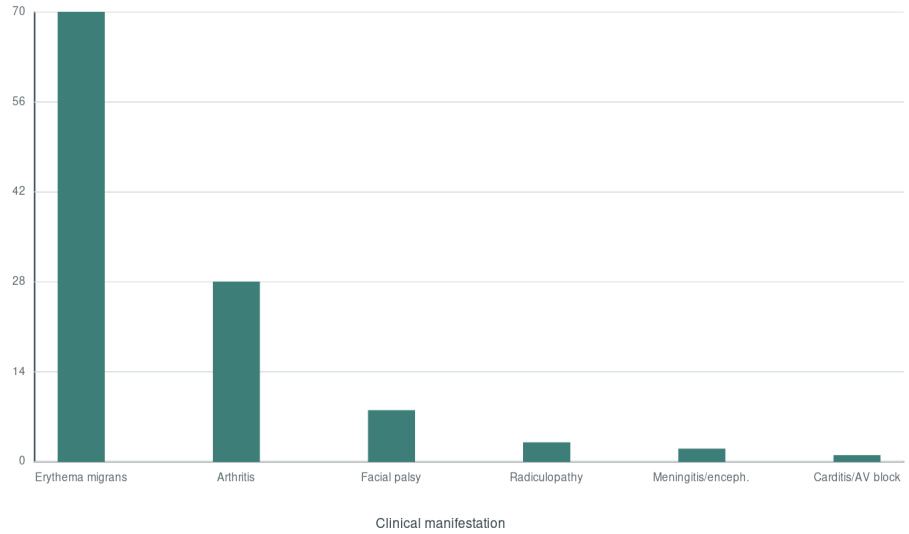

Figure 8. Frequency of clinical manifestations among reported cases

Erythema migrans is by far the most common objective manifestation; carditis is rare. Percentages exceed 100% because some patients have more than one manifestation. Values are representative of CDC surveillance data.

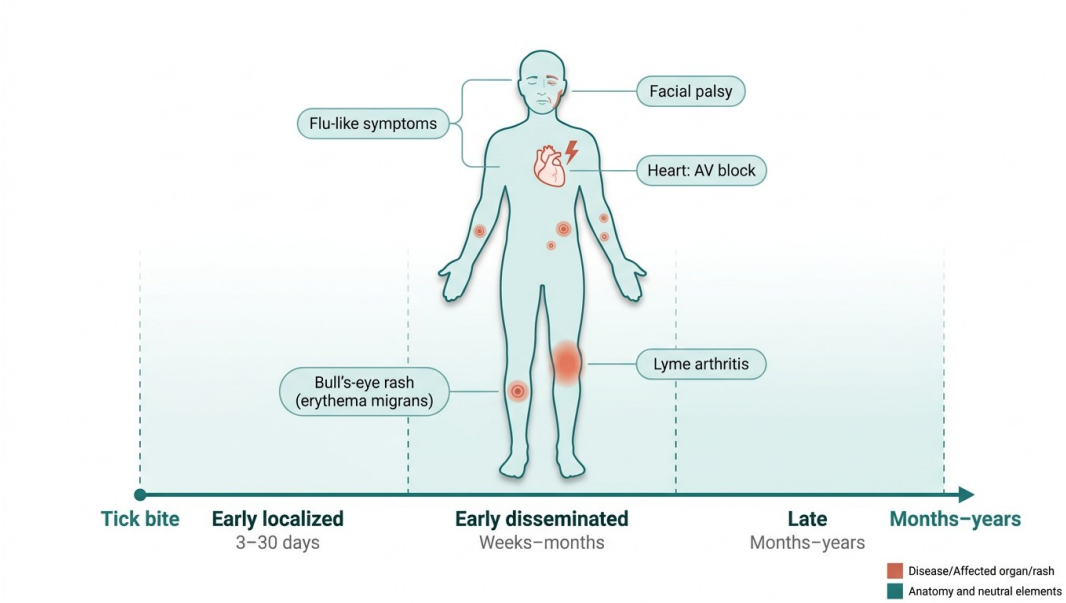

Figure 9. Stages of Lyme disease across the body and over time

From the tick bite, disease may progress through early localized (erythema migrans, flu-like illness), early disseminated (facial palsy, carditis with AV block, multiple lesions), and late (Lyme arthritis) stages. Most patients are treated and cured before later stages occur.

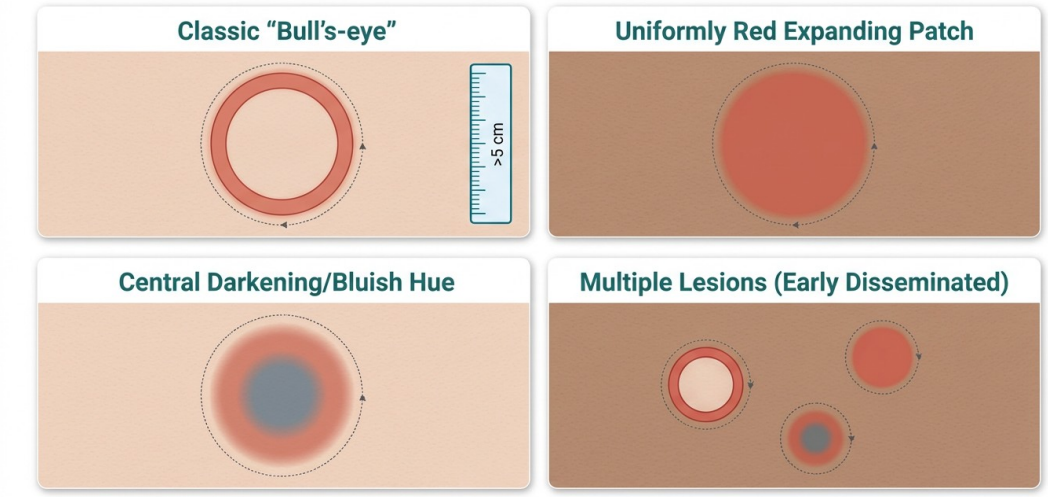

Figure 10. Recognizing erythema migrans (the rash)

Erythema migrans is variable: the classic central-clearing 'bull's-eye', a uniformly red expanding patch, a lesion with central darkening or a bluish hue, or multiple lesions in early disseminated disease. It is often neither itchy nor painful, and many patients do not recall a tick bite.

Mechanistic depth — for scientists

Tissue tropism and the inflammatory phenotype are shaped by genospecies, strain (e.g., OspC and RST genotypes correlate with dissemination), and host immunogenetics. [3,9]Antibiotic-refractory Lyme arthritis illustrates a post-infectious, immune-mediated mechanism: in a subset of patients, synovitis persists after spirochaetal killing, associated with HLA-DR alleles, heightened interferon responses, impaired regulatory T-cell function, and proposed autoreactivity, and it responds to anti-inflammatory or immunomodulatory therapy rather than further antibiotics. [13,9] The autoimmune hypothesis is supported by associations with HLA-DR alleles (e.g., DRB1*0401) and by the identification of candidate self-antigens — including endothelial cell growth factor and annexin A2 — that are targets of T- and B-cell responses in antibiotic-refractory disease. [31,32]

Table 2. Stages of Lyme disease: timing, features, and typical first-line therapy

Stage	Typical timing after bite	Key manifestations	Representative first-line therapy
Early localized	3–30 days	Single erythema migrans; flu-like symptoms	Oral doxycycline 10–14 days (or amoxicillin/cefuroxime)
Early disseminated	Weeks–months	Multiple EM; cranial neuropathy; meningitis; carditis	Oral doxycycline; IV ceftriaxone for high-grade carditis or CNS disease
Late	Months–years	Lyme arthritis (esp. knee); rarely encephalomyelitis	Oral antibiotics 28 days; reassess for antibiotic-refractory arthritis

Therapy summarized from the 2020 IDSA/AAN/ACR guideline; durations are representative and individualized in practice.

5. Diagnosis

At a glance — for general readers

If you have the classic bull's-eye rash and have been somewhere ticks live, a doctor can diagnose Lyme disease just by looking — no blood test is needed at that point. [10] For later symptoms, blood tests that detect your body's antibodies are used. These tests are not perfect, especially in the first days of infection, which is why doctors weigh your symptoms and exposure rather than relying on a test alone. [14]

Clinical detail — for physicians

EM in an endemic setting is a clinical diagnosis; do not order serology, which is insensitive in the first 1–2 weeks before seroconversion. [10,14]For extracutaneous and later disease, use standardized two-tier testing. The traditional algorithm is an enzyme immunoassay (EIA) followed, if positive or equivocal, by IgM/IgG immunoblot. [14] The FDA-cleared modified two-tier testing (MTTT) approach replaces the immunoblot with a second, different EIA and is now widely used (Figure 11). [14,15] IgM reactivity alone should not be used to support a diagnosis of illness lasting more than ~30 days because of poor specificity in that setting. [4,14]

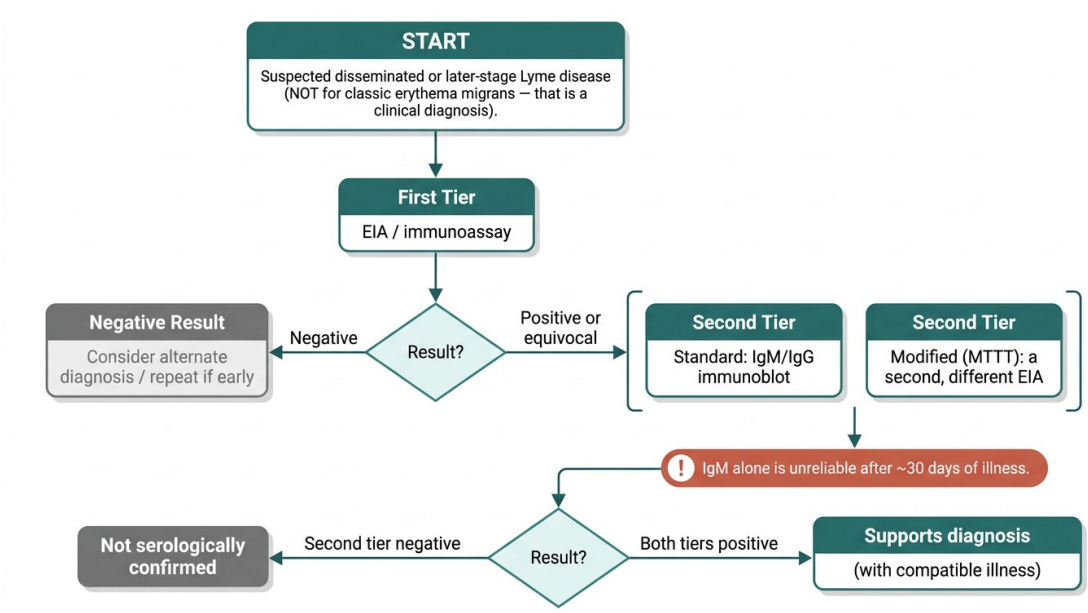

Figure 11. Standardized two-tier serologic testing algorithm

Two-tier testing for disseminated or later-stage disease (not for classic erythema migrans, a clinical diagnosis): a first-tier EIA, and if positive or equivocal, either an IgM/IgG immunoblot (standard) or a second EIA (modified two-tier). IgM alone is unreliable after about 30 days of illness.

Mechanistic depth — for scientists

Serology measures the host antibody response, not the organism, so it cannot distinguish active from past infection and remains positive after cure — a fundamental limitation for test-of-cure and for evaluating persistent symptoms. [14,16] Direct detection (culture, PCR) is insensitive in blood because spirochaetaemia is low and transient, though synovial-fluid PCR can aid Lyme arthritis and CSF analysis (pleocytosis, intrathecal antibody, CXCL13) supports neuroborreliosis. [14,16] Emerging approaches — next-generation immunoassays using recombinant/peptide antigens, metabolomic and transcriptomic signatures, and improved direct-detection assays — aim to shorten the early-window diagnostic gap. [15]

Table 3. Common diagnostic modalities for Lyme disease

Modality	Best use	Key caveat
Clinical recognition of EM	Early localized disease in endemic area	Rash may be atypical; not all patients recall a bite
Standard two-tier serology (EIA → immunoblot)	Disseminated / late disease	Insensitive in first 1–2 weeks; stays positive after cure
Modified two-tier (EIA → EIA)	FDA-cleared alternative to immunoblot	Interpretation still depends on pre-test probability
PCR	Synovial fluid/tissue in Lyme arthritis	Low yield in blood; not a test of cure
CSF (pleocytosis, intrathecal Ab, CXCL13)	Suspected CNS neuroborreliosis	Not useful for peripheral nervous system disease

Sources: Branda & Steere 2021; Guérin et al. 2023; Halperin 2019; Lantos et al. 2021.

6. Treatment

At a glance — for general readers

Lyme disease is treated with antibiotics, usually taken by mouth for two to four weeks. The large majority of people recover completely, especially when treatment starts early. [3,8] Severe heart or nervous-system involvement may need antibiotics given through a vein, but even then the outlook is generally good. [4]

Clinical detail — for physicians

Oral doxycycline is first-line for most presentations, including EM (10–14 days) and most early neurologic disease in ambulatory patients; amoxicillin and cefuroxime axetil are alternatives. [8,4] Doxycycline is no longer contraindicated for short courses in young children. Intravenous ceftriaxone is reserved for high-grade carditis, meningitis/parenchymal CNS disease, and selected refractory cases. [4] Lyme arthritis is treated with a 28-day oral course; persistent synovitis after adequate antibiotics is managed as antibiotic-refractory (post-infectious) arthritis with DMARDs/anti-inflammatories or synovectomy, not repeated antibiotics. [13,4]

Mechanistic depth — for scientists

B. burgdorferi has no known resistance to first-line agents, and clinical relapse after guideline-concordant therapy is rare. Reports of in-vitro 'persister' subpopulations tolerant to antibiotics have driven interest in novel or combination regimens, but no controlled clinical trial has shown that such regimens improve patient outcomes, and several proposed agents (e.g., disulfiram) carry meaningful toxicity. [18,20] Animal studies complicate the picture: experimental models show that borrelial nucleic acids and occasionally non-cultivable spirochaetes can be detected after antibiotic treatment, and xenodiagnosis has been explored to probe for residual organisms, yet systematic appraisal finds insufficient evidence that viable, infectious spirochaetes survive adequate therapy. [29,30,37] The central translational question remains whether any persistent symptoms reflect ongoing infection (not demonstrated in humans by current methods) versus post-infectious immunologic or other mechanisms. [20,21]

Table 4. Representative antibiotic regimens (adapted from the 2020 IDSA/AAN/ACR guideline)

Presentation	Preferred regimen	Typical duration
Erythema migrans	Doxycycline PO (alt: amoxicillin, cefuroxime axetil)	10–14 days (doxycycline 10)
Early neurologic (e.g., facial palsy, meningitis, ambulatory)	Doxycycline PO	14–21 days
Lyme carditis (high-grade AV block / hospitalized)	IV ceftriaxone, transition to oral	14–21 days total
Lyme arthritis	Doxycycline or amoxicillin PO	28 days
Post-exposure prophylaxis (qualifying high-risk bite)	Single-dose doxycycline 200 mg	Single dose within 72 h

Regimens are representative; clinicians should consult the current full guideline and individualize by age, pregnancy, allergy, and severity.

7. Post-treatment Lyme disease syndrome and the “chronic Lyme” debate

At a glance — for general readers

A minority of people continue to feel unwell — tired, achy, or foggy — for months after their Lyme disease has been treated. This is real and can be disabling. Studies have repeatedly shown, however, that taking antibiotics for long periods does not relieve these symptoms and can cause harm, so care focuses on managing symptoms and supporting recovery. [20,21,15]

Clinical detail — for physicians

Post-treatment Lyme disease syndrome (PTLDS) describes fatigue, musculoskeletal pain, and cognitive complaints persisting >6 months after documented, adequately treated Lyme disease, with functional impact. [21] It must be distinguished from the broader, poorly defined label 'chronic Lyme disease,' which is often applied to patients without objective evidence of prior infection. [22] Multiple randomized controlled trials show prolonged antibiotics confer no durable benefit and carry real risk (e.g., line-associated complications). [19,20] In a prospective human study, xenodiagnosis using laboratory-reared *Ixodes scapularis* larvae found no evidence of *B. burgdorferi* in treated patients regardless of symptom status, arguing against ongoing infection as the explanation for persistent symptoms. [35] Management is supportive and multidisciplinary; clinicians should validate symptoms while avoiding ineffective and potentially harmful 'chronic Lyme' protocols. [20,22,17]

Mechanistic depth — for scientists

Reported prevalence of persistent symptoms after treatment varies widely with case definition and ascertainment. [20,17] Proposed mechanisms include residual tissue damage, persistent microbial antigens or 'debris,' immune dysregulation and autoimmunity, altered neural processing of pain and fatigue, and unrelated comorbidities; persistent culturable infection in humans has not been demonstrated with current methods. [20,21,35] Well-phenotyped longitudinal cohorts, validated biomarkers, and standardized outcome measures are needed to resolve mechanism and to test rationally targeted (non-antibiotic) interventions. [7,18,17]

8. Prevention: personal, environmental, and vaccines

At a glance — for general readers

The best protection is avoiding tick bites: use EPA-registered repellents, treat clothing or gear with permethrin, wear long clothing in tick habitat, and do a thorough tick check after being outdoors. [4,8] Removing an attached tick promptly and properly — grasping it close to the skin with fine tweezers and pulling straight out — greatly lowers the chance of infection, because the tick usually must be attached for a day or more to transmit the bacteria (Figure 12). [4,5]

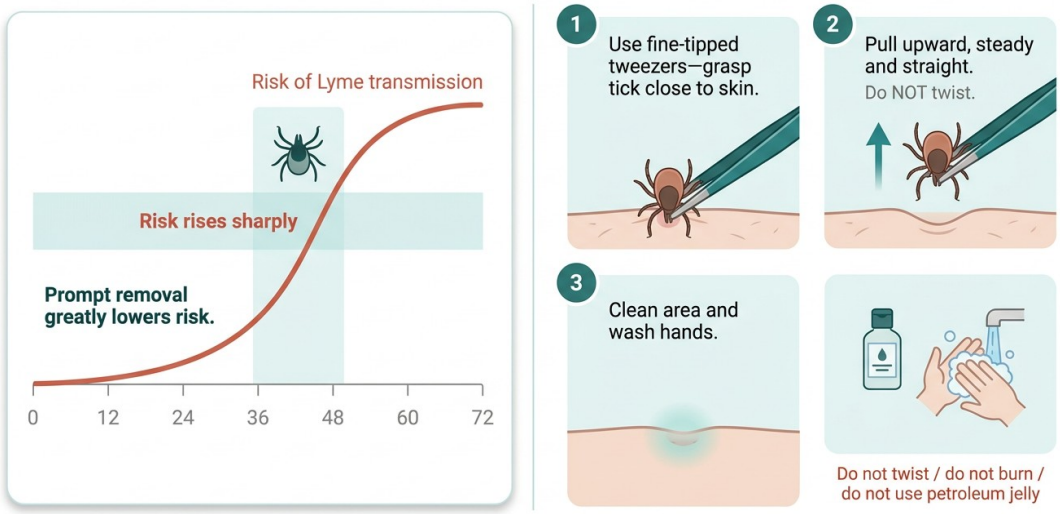

Figure 12. Transmission risk by attachment time, and safe tick removal

The risk of Lyme transmission rises sharply once an infected tick has been attached for roughly 36–48 hours, so prompt, correct removal markedly lowers risk: grasp the tick close to the skin with fine-tipped tweezers and pull straight up — do not twist, burn, or apply petroleum jelly.

Clinical detail — for physicians

For a qualifying high-risk *I. scapularis* bite (identified, attached ≥36 hours, in a highly endemic area, prophylaxis startable within 72 hours, no contraindication), a single 200 mg dose of doxycycline reduces the risk of Lyme disease; meta-analysis supports the single-dose strategy. [4,23] Routine antibiotic treatment of asymptomatic bites that do not meet these criteria is discouraged. The full layered approach to prevention — from personal protection to vaccination — is summarized in Figure 13. [4]

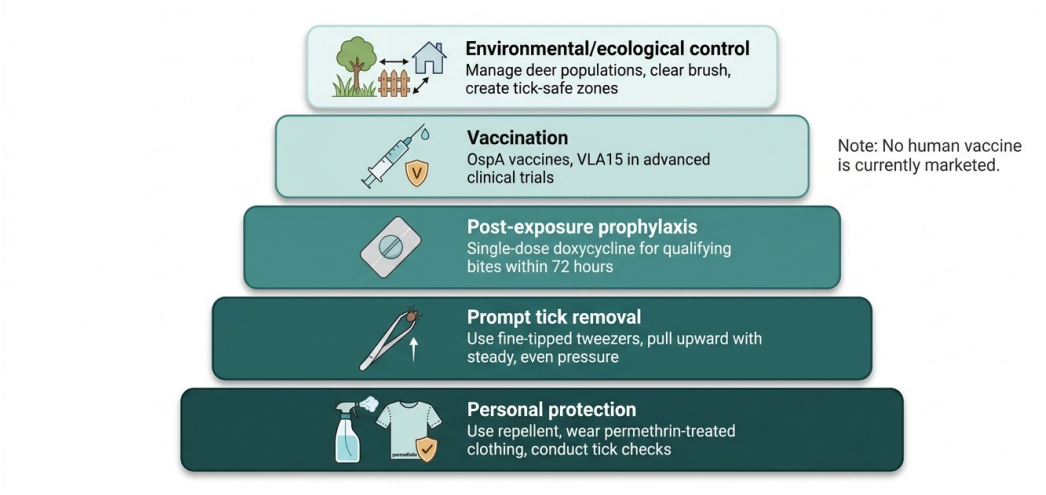

Figure 13. Layers of Lyme disease prevention (defense in depth)

Prevention is layered: personal protection (repellents, permethrin-treated clothing, tick checks), prompt tick removal, post-exposure prophylaxis for qualifying bites, vaccination (OspA vaccines; VLA15 in trials), and environmental/ecological control. No human vaccine is currently marketed.

Mechanistic depth — for scientists

The first human vaccine, LYMErix (recombinant OspA), demonstrated efficacy but was withdrawn in 2002 amid low uptake and unsubstantiated safety concerns. OspA acts unusually — antibodies are ingested by the feeding tick and kill spirochaetes in the midgut before transmission ('transmission-blocking', Figure 14) — and whole-cell first-tier serology could be confounded by vaccine-induced anti-OspA antibodies, a lesson informing current assay and vaccine design. [3,34] The leading next-generation candidate, the hexavalent VLA15 (OspA serotypes 1–6), was safe and immunogenic across all serotypes in a randomised phase 1 trial and has advanced into late-stage clinical evaluation; anti-tick ('vector') vaccine strategies targeting tick salivary proteins and reservoir-targeted ecological interventions are also under study. [33,5]

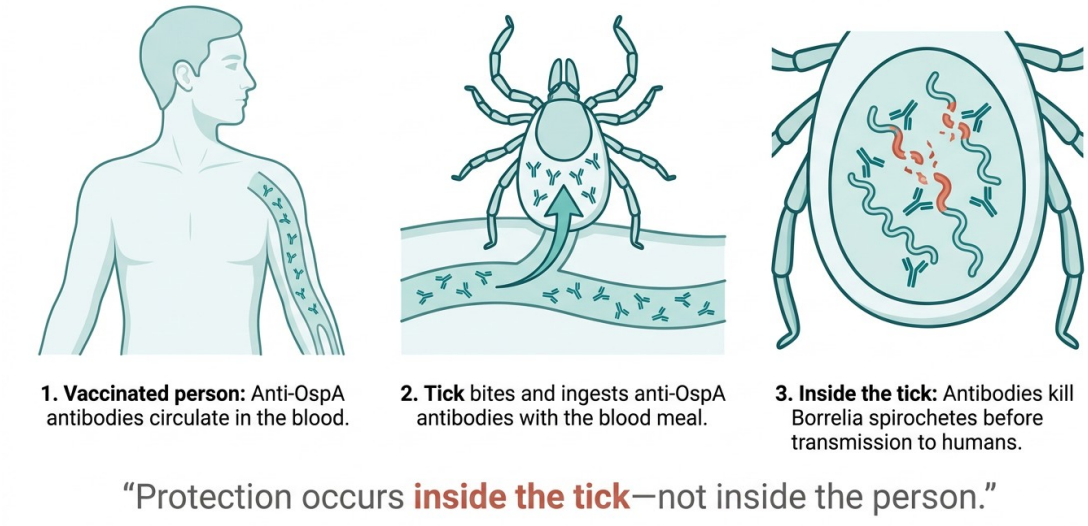

Figure 14. How an OspA vaccine works: transmission-blocking immunity

Anti-OspA antibodies in a vaccinated person are ingested by a feeding tick and kill Borrelia inside the tick gut before the spirochaete can be transmitted — so protection occurs inside the tick, not the person.

Table 5. Layers of Lyme disease prevention

Layer	Examples	Evidence / status
Personal protection	DEET/picaridin repellents; permethrin-treated clothing; tick checks	Recommended; reduces bites
Prompt tick removal	Fine-tipped tweezers, steady upward traction	Risk rises after ~36–48 h attachment
Post-exposure prophylaxis	Single-dose doxycycline for qualifying bites	Supported by RCT/meta-analysis
Vaccination	OspA (LYMErix, withdrawn 2002); hexavalent VLA15 in clinical trials	No vaccine currently marketed for humans; VLA15 safe/immunogenic in phase 1
Environmental / ecological	Landscape management; host-targeted acaricides	Variable, area-dependent effectiveness

Sources: Lantos et al. 2021; Zhou et al. 2021; Kullberg et al. 2020; Steere et al. 2016.

9. Special populations

At a glance — for general readers

Children are among those most often affected, partly because they play outdoors. The illness in children is treatable and most do very well. People who are pregnant can also be treated safely with appropriate antibiotics. [24]

Clinical detail — for physicians

Incidence is highest in children aged 5–9 years; EM is the most common presentation, and most pediatric Lyme disease is cured with short oral courses. [24] Doxycycline is now considered acceptable for short courses across pediatric ages. In pregnancy, recommended regimens (e.g., amoxicillin; doxycycline avoided) are effective, and adverse fetal outcomes from appropriately treated maternal Lyme disease have not been substantiated. [4,24]

Mechanistic depth — for scientists

Pediatric outcome data are reassuring, including for facial palsy and Lyme meningitis, although recovery from late neurologic disease can be slower. [11,24] Questions remain regarding optimal antibiotic stewardship, the natural history of subclinical infection, and immune correlates of protection relevant to pediatric vaccination strategies. [18,24]

10. Climate change and the shifting geography of risk

At a glance — for general readers

Warmer temperatures and changing seasons are letting ticks survive in more places and stay active longer, so Lyme disease is appearing in areas where it used to be rare, including parts of Canada. This means more people may be at risk in the years ahead. [25,26]

Clinical detail — for physicians

The geographic footprint of *I. scapularis* and of human Lyme disease has expanded northward and into new counties over recent decades. Clinicians in newly endemic and 'emerging' areas should raise their index of suspicion and update their pre-test-probability assumptions accordingly. [2,26]

Mechanistic depth — for scientists

Both phenomenological (climate-envelope) and mechanistic models predict continued range expansion of *Ixodes* ticks and tick-borne disease under warming, though projections are sensitive to assumptions about host dynamics, humidity thresholds, and land use. [26,39,40] Climate change is best understood as one driver within a web of interacting ecological and anthropogenic factors (host community composition, landscape fragmentation, biodiversity); attribution and prediction remain active research areas with direct public-health-planning implications. [25,26]

11. Public-health implications and future directions

Lyme disease sits at the intersection of clinical medicine, ecology, and public-health policy, and progress requires advances on several fronts at once.

- Surveillance: automated extraction from electronic health records and laboratory data can complement case reporting and better capture true burden, complications, and persistent symptoms.
- Diagnostics: assays that detect early infection and that can distinguish active from past infection would transform both clinical care and the study of persistent symptoms.
- Therapeutics and vaccines: a marketed human vaccine (e.g., a successful VLA15) and rationally targeted treatments for post-infectious symptoms remain major unmet needs.
- Equitable, sustained research funding has historically lagged the disease burden, slowing progress on these questions.

Taken together, these priorities reflect a maturing recognition that controlling Lyme disease is as much an ecological and systems challenge as a clinical one. [2,7,18]

12. Conclusion

Lyme disease is common, expanding, and — when recognized early — highly treatable. [1,3] The core clinical message is durable: recognize erythema migrans, treat promptly with first-line oral antibiotics, reserve serology and intravenous therapy for the situations where they help, and avoid prolonged antibiotics for persistent post-treatment symptoms. [4,8,20] The frontier lies in earlier and more specific diagnostics, an effective human vaccine, a mechanistic understanding of post-treatment symptoms, and public-health systems that can keep pace with a changing climate and landscape. [7,18,25]

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