Ticks. Just seeing or hearing the word is enough to make your skin crawl. And with good reason. Not just a blood-sucking nuisance, ticks transmit potentially bad diseases, including Lyme disease, Rocky Mountain spotted fever, relapsing fever, tularemia, tick-borne meningoencephalitis, Colorado tick fever, babesiosis, anaplasmosis (ehrlichiosis), and rarer diseases including Crimean-Congo hemorrhagic fever, cytauxzoonosis, Heartland Virus, deer tick virus (Powassan virus lineage II), and Bourbon Thogotovirus, discovered in 2015. Most of these are very rare, but some can be fatal and there is no treatment. We will cover ticks and diseases most common in the US, particularly the Northeast, mid-Appalachians and upper Midwest. But ticks that can carry Lyme disease are even showing up on California beaches, so much of this information applies widely. *https://www.npr.org/2021/06/11/1005391496/lyme-disease-carrying-ticks-are-turning-up-on-californias-beaches

**Meet the Ticks**

Ticks have been around for 100 million years, so it’s no surprise that there are almost 2000 species of them. But in North America, depending on how you count them, there are three or four main ticks of medical concern.

*Ixodes scapularis,* the deer tick or black-legged tick (or, in the upper Midwest, bear tick), also known as *I. dammini,* is a member of the *Ixodidae* family of hard-bodied ticks. It is the main vector for human Lyme disease. A black-legged tick species in northern California and Oregon, *Ixodes pacificus,* also transmits Lyme disease, and only an entomologist or maybe another tick can tell the two species apart. The adult black-legged tick is fairly large and easy to see, but most cases of early Lyme disease occur during the late spring and summer, when the nearly-invisible nymph is seeking a blood meal. And, 20% of ticks are in areas you can’t see on yourself, so it’s common to get Lyme disease without noticing a tick bite. Black-legged ticks also transmit anaplasmosis and babesiosis.

*Dermacentor variabilis,* the American dog tick, transmits Rocky Mountain Spotted Fever, tularemia and anaplasmosis. It’s found across pretty much everywhere east of the Rocky Mountains and in coastal California.

*Amblyomma americanum,* the lone star tick, which transmits STARI or Master’s disease (very similar to Lyme Disease, see below), is found in the southeast US up through the Mississippi Valley and through the Appalachians up into New England.

*Haemaphysalis longicornis,* the Asian longhorned tick, has recently (November 2017) migrated to the mid-Atlantic/mid-Appalachian states, and there are horror stories about massive numbers of these ticks attacking cattle, but they are not known (yet) to transmit human disease in North America.
**Preventing Tick Attachment**

Assuming you don’t want to wear a flea and tick collar, which doesn’t work as well without a built-in fur coat, you may want to investigate other methods to prevent tick attachment when outdoors.

There are a variety of chemicals that you can put on your skin to prevent tick (and insect) bites. There is some information in the medical literature, but the best information comes from ongoing testing performed by Consumer Reports (http://consumerreports.org). “Other” ingredients in insect repellents are just as important as the listed “active” ingredients. Those “inactive” ingredients may make the active ingredients work better or last much longer on your skin. So, it turns out that for insect repellents, brand names are just as important as the “active ingredient” or its concentration, but it is worth considering the “active ingredients” before turning to specific brands.

DEET is the most famous and highly effective, but is mildly toxic, especially in kids. It’s greasy on the skin, and turns nylon and many plastics to a disgusting sticky goo. The American Academy of Pediatrics advises against using repellents with DEET concentrations higher than 30 percent on children, and Consumer Reports says that nobody needs anything more than 30%.

Picaridin was invented by Bayer and is made by the Lanxess Corporation of Pittsburgh. It is much less greasy on the skin than DEET and doesn’t dissolve nylon or plastics. It is about the same as DEET for protection against ticks. In one study of anopheles mosquitoes, picaridin was more effective than DEET; picaridin is also a bit more effective than DEET for northern biting black flies. Though DEET is only mildly toxic, picaridin seems to be less toxic. Picaridin is my choice for an active ingredient. It’s a bit more expensive than DEET, which is why Consumer Reports doesn’t rate it as highly as some DEET preparations, but to me it’s worth it. Choose a preparation with a vehicle that allows it to persist on the skin; Sawyer Premium 20% Picaridin brand lasts 10-12 hours but other brands (and the Sawyer picaridin lotion) don’t last as long.

Oil of lemon eucalyptus is found in the leaves of *Eucalyptus citriodora* although chemically synthesized. It is marketed under the brand name Repel. It is as effective as 30% DEET. But it smells very strong. There is also a Repel version that is “scented” and combines 15% DEET with “other ingredients” which one suspects might be oil of lemon eucalyptus; unlike other 15% DEET preparations, it is just as effective as 30% DEET. This is quite unlike other “herbal” repellents that are essentially useless.

Skin So Soft is a bath oil sold by Avon. In the 1990s, an urban legend arose that it repelled mosquitoes and ticks. As with other urban legends about mosquitoes (e.g., Bounce fabric softener, Vick’s VapoRub, Lemon Joy detergent and extract of vanilla – see snopes.com for more on urban insect-repellent legends), it turned out to be totally bogus. Consumer Reports tested Skin So Soft and found it ineffective as did a study by Fradin (protected against mosquito bites for only 10 minutes). However, the urban legend persisted, and Avon wasn’t going to pass up a sales and marketing opportunity like this, so they did the smart thing: they offered a version called Skin So Soft Bug Guard with citronella in it, which unfortunately was no better than the original and quickly discontinued. So, then they came out with a version containing picaridin, which is effective as described above, although not nearly so good as many 30% DEET preparations or my favorite Sawyer picaridin spray, and then a version with:

IR3535 which is a newer repellent that is nice on the skin and doesn’t dissolve your nylon clothes. It’s highly effective against ticks for up to 12 hours at 20% concentration, though it’s not nearly as effective against mosquitoes as picaridin or DEET. It’s available as Avon Skin So Soft Bug Guard Plus IR3535, which, despite the confusingly similar name has IR3535 instead of Bug Guard Plus’s picaridin. There is also version which, in addition to 20% IR3535, includes sunblock, a bad combination according to the CDC and Consumer Reports. Why? Because you should apply insect repellent sparingly (due to potential toxicity) and you should apply sunscreen liberally and frequently. None of the Avon bug repellents are rated highly by Consumer Reports.

Safety: DEET, if you use lower concentrations, is considered safe on kids > 2 months old, picaridin is considered safe on all children and infants but in lower (10%) concentrations, and oil of lemon eucalyptus is not supposed to be used in children under 3 years of age. All the above repellents and permethrin (see below) are considered safe in pregnancy.

**Bottom line:** Use the Sawyer 20% picaridin spray. I repackage mine in small (30-60 mL = 1-2 oz) Nalgene bottles, available from amazon.com, for outdoor recreation and search and rescue and disaster responses. It’s not as convenient as the spray,

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* Consumer Reports, Volume 58, No. 7, July, 1993, pages 451 - 454
but much less likely to leak all over the inside of your pack. You can pour a bit into your hand and then rub it on your skin. Or, use one of the 25-30% DEET or lemon eucalyptus oil preparations highly recommended by Consumer Reports in May 2021: Repel Lemon Eucalyptus Insect Repellent or Cutter Lemon Eucalyptus Insect Repellent Aerosol.

It’s also possible to treat clothing with the “repellent” permethrin. It doesn’t repel ticks; it kills them before they can bite you. In low concentrations, as on treated clothing, it’s quite nontoxic to mammals. You can treat clothes at home with a simple spray that will last 6 washings, buy clothing pretreated with permethrin that will last through 70 washings, or send your own clothing to Insect Shield to get that 70-wash treatment. It reduces tick bites by about 3/4, as ticks climb up your legs from the ground. My whole family treated pairs of socks this way, but not our outdoor pants, as you have to remove any DWR (durable water-repellent) treatments from your pants by dry cleaning before Insect Shield can bond the permethrin to pants. LL Bean sells a lightweight, very breathable summer windshirt with hood with the Insect Shield treatment to prevent mosquito bites (No Fly Zone Jacket). I got one as an impulse buy one day and it seems to work great on hot, humid summer evenings during “mosquito hour.”

Removing Ticks

There are many ways to remove ticks. Some are bad. For example, smothering a tick with Vaseline or goosing it in the rear end with a hot, just-blown-out-match probably isn’t such a good idea; not only is this poor at persuading the tick to let go, but it may make it vomit into your skin. You want to avoid ripping the body off, leaving the head embedded in the skin. However, when ticks have been embedded for a while, they glue their heads into the skin, some species more than others. Even the best removal methods sometimes leave the head in.

Grabbing at the neck with a pair of blunt forceps and gently pulling until the jaws tire and the entire tick comes out is best according to multiple authorities including the Centers for Disease Control and Prevention (CDC), but based on small human studies.12-14 There are a variety of devices for tick removal. I have tried the Tick Key but couldn’t get it to work at all. I have used the Tick Plier (previously known as the Tick Nipper). The Tick Plier works better than the Tick Key, but sometimes it just can’t get out a tick. There is a device called the Tick Twister that uses a twisting technique that, in a large, high-quality veterinary 2006 study, was found to be superior to all other methods, including the tweezers method recommended by the CDC.15 I’ve used the Tick Twister like the Tick Key to simply pull out ticks, and it works better than the Tick Key or Tick Plier, but it works best with a twisting motion. There is a Tick Twister Pro for ticks on animals, and a set of two smaller ones for humans; I usually use the Pro version on humans, and I find it usually works as it’s easier to grip than the smaller “human” ones, but sometimes for tiny ticks I have to use the smaller human versions.

Plenty of people come to the ED with embedded tick heads. The best way I’ve found to get out an embedded tick head is to grab it with a pair of Adson (toothed) forceps, pull, then delicately cut around it with a #15 scalpel blade, then apply a Band-Aid and bacitracin ointment. One author recommends an elliptical incision followed by a suture (even for intact ticks) but I prefer to excise very narrowly and shallowly then leave open to avoid infection. One author recommends a biopsy punch,17 but one’s seldom available in the ED. Sometimes, you can just pull out the head with a pair of splinter forceps.

Lyme disease

Lyme disease is common. The CDC estimates “476,000 Americans are diagnosed and treated for Lyme disease.” It is the most common tick-borne disease in the northern hemisphere. The big state of Pennsylvania has the most reported cases (6763 confirmed + 2235 probable in 2019),† about a third of cases, and more than any other state, but smaller Vermont is where you’re most likely to get it. But the CDC estimates that only about 10% of Lyme disease is reported. And, the incidence is increasing. In Pennsylvania, Lyme Disease is endemic: 39%

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* https://www.cdc.gov/lyme/stats/humancases.html
† https://www.cdc.gov/lyme/stats/tables.html
of southwestern PA nympha blacklegged ticks are infected.19

Lyme disease can get very complicated; we have to get into a bit of genetic microbiology, but I’ll try to keep it simple. The original spirochete (long twisty squiggly bacterium) was given the species name *Borrelia burgdorferi* after Willy Burgdorfer, who identified it as the cause of Lyme disease in 1982. But microbiologists now talk not about a single species but "*Borrelia burgdorferi sensu lato complex*” (Bbsl) or "*Borrelia burgdorferi sensu stricto*". “Sensu lato” is Latin for “in the broad sense” and “sensu stricto” means “in the strict sense.” This reflects the effects of genetic analysis on the definition of species, and the fight between lumpers and splitters as far as whether a genetically slightly different version of *Borrelia burgdorferi* is part of the same species or a different species. For example, a recent article is entitled “*Borrelia mayonii* sp. nov., a member of the *Borrelia burgdorferi sensu lato complex*, detected in patients and ticks in the upper midwestern United States.”20 My interpretation: “Hey, I found this thing that’s sorta like what Burgdorfer found but different enough that I want to give it a different species name. Whaddya think?” Some also suggest that instead of saying “*Borrelia burgdorferi sensu lato complex*” we should simply say “Lyme borrelia.”

About 20 Bbsl genospecies have been identified. What, you may ask, is a genospecies? Wiktionary says it means: A species (group of organisms that can interbreed) identified and characterised by means of genetics. We now know there are now numerous species of *Borrelia burgorferi-ish* bacteria in the US: *B. burgdorferi sensu stricto* (s.s.), *B. americana*, *B. andersonii*, *B. californiensis*, *B. carolinensis*, and *B. kurtenbachii*. *B. burgdorferi s.s.*, *B. bissettii*, and *B. carolinensis* also appear in Europe. Now, if the other microbiologists don’t object too loudly, the *B mayonii* of the article title above will join them. Only a few of them infect humans. *Borrelia mayonii* is one that infects people in the upper Midwest (Wisconsin-ish), in at least the six people that we know about. They had high levels of spirochetes in the blood, a diffuse macular (non-bumpy) red rash and not a localized target lesion like *B burgdorferi s.s.*, fever, vomiting and neurological symptoms not otherwise specified.21 But six patients is not a very big sample from which to generalize. And in the lumper-vs-splitter divide, it’s worth noting that the desire to publish articles about new species for academic advancement argue for more rather than fewer species. Jus’ sayin’.

A variant of Lyme disease with different characteristics and caused mostly by *Borrelia afzelii* occurs in Europe and Scandinavia.22 There, erythema migrans (see below) is more chronic and people sometimes get acrodermatitis chronica
atrophicans (a “tissue paper–like cutaneous atrophy”). There are also other *Borrelia*, carried by ticks of the same *Ixodes ricinus* complex to which American black-legged ticks belong, that cause similar borreliosis in eastern Europe and Asia (B. afzelii, B. bavariensis, B. garinii, B. japonica, B. lusitaniae, B. sinica, B. spielmanii, B. tanukii, B. turdi, B. valaisiana, and B. yangtze).

**Lyme Ecology**

There is discord between hunting and animal rights groups about the role of deer culling in controlling Lyme disease which seems to have nothing to do with the evidence. What the evidence shows is that decreasing the deer population actually increases Lyme disease, likely by increasing nymphal ticks feeding on mice.14 That makes me feel better as sometimes we trap mice in our basement, and in my neighborhood, where I live right next to a borough park, I see about 4-5 deer every day, sometimes more. Sometimes they are blocking my driveway and I have to honk the horn to get them out of the way to get into the garage.

A higher population of *foxes*, though, given they hunt mice, decreases Lyme Disease, surprisingly not by decreasing the mouse population, but probably by making them more careful in their movements and decreasing the number of ticks on them (~10%).25

Indeed, the incidence of Lyme disease reflects the population of the white-footed mouse, *Peromyscus leucopus*. In the short term, mouse population and Lyme incidence is determined by the number of acorns two years prior.26 There is well-known phenomenon called a “mast year,” when oaks across the entire continent produce about 10 times their normal yearly crop of acorns. There are two different groups of oaks that mast on separate schedules, those with pointy leaves and those with rounded leaves. Mast years are irregular, probably as a reproductive strategy of “predator satiation”: keeping production down to control the number of acorn-eating animals, then suddenly producing many more acorns than the squirrels, mice and deer can eat. The environmental trigger, or mode of communication among oak trees, is totally unknown. Other tree species also exhibit mast years, not synchronized with the oaks.

I live in the Pittsburgh area which is now a hotbed of Lyme disease. Even Pittsburgh’s city parks (which, admittedly, are some of the largest and “wildest” of any major city) are full of Lyme-disease carrying ticks. During the 2017 season, I saw about 50 patients with Lyme disease, once four cases in two hours. Some of them were sick enough to require IV antibiotics. From 2000 to 2014, the incidence (per 100,000 people) increased from 1.4 to 41.5, and the figures are even worse north towards Erie. This spread is occurring elsewhere, for instance the Lyme incidence is rapidly increasing in Maine, likely from similar effects. And the CDC numbers are far below how often Lyme occurs, as only a fraction of cases are reported. For instance, in 2011-2013, CDC surveillance reported 22 cases in my home Allegheny County, PA, whereas a retrospective review just of *pediatric cases* at Children’s Hospital in Pittsburgh from the same period found 221 cases, and of interest, most of the cases are now from urban and suburban areas.27

The first factor in the exponential growth in Lyme disease is the repopulation of areas with blacklegged ticks from reservoirs in the coastal northeast. Both primary hosts for the blacklegged tick, the white-tailed deer and the white-footed mouse, prefer to live along the forest’s edge; ecologists call this the forest-field ecotone. In the 1600s, with the die-off of indigenous people from introduced European diseases, abandoned native farms became covered with nearly continuous woodlands, destroying the deer, mouse and blacklegged tick’s ecotone habitat. In the 1800s, European immigrants started farming areas away from the main coastal cities, likely once again increasing the number of deer, mice and ticks, but by the late 1800s, central and western Pennsylvania in particular had become the main source of the nation’s lumber. Essentially all of the area was clear-cut for lumber, again destroying the tick’s host habitat. In the era from about 1890 to 1930, efforts to protect these devastated lands resulted in national and state forests, where sustainable forestry was the watchword. During this period, families also abandoned their farmland to move to the cities, both these factors resulting in a rapid reforestation of much of Pennsylvania. But with this reforestation and loss of small farms, again the blacklegged tick’s forest-field ecotone habitat disappeared.

But throughout the later twentieth century and now into the twenty-first, the forest-field ecotone habitat throughout eastern North America has mushroomed in size, thanks to suburban sprawl and strip malls. This has massively increased the white-footed mouse population.26

Not only are the white-footed mouse and its tick hangers-on spreading, but *Borrelia burgdorferi* seems to be spreading as well. Perhaps it’s just *B burgdorferi* finally catching up with the tick expansion, but for whatever reason, in areas like western Pennsylvania and Maine, the percentage of blacklegged ticks infected with the spirochete is rising as well.28

Some people are so concerned about ticks and Lyme disease that they ask me about how to eradicate ticks from their yards: spraying the entire yard with insecticide? Bad idea, you’re more likely to get sick from the insecticide than from the ticks, and the insecticide will go away with the first rainstorm. The CDC says the insecticide will reduce the number of ticks but not make you less likely to get Lyme Disease. There are better ideas.

First, back in 1987, Thomas Mather at the University of Rhode Island Tick Encounter Resource Center developed a “drive-through” mousetrap (Thermacell Tick Control Tubes) that allows mice to carry permethrin-treated cotton balls back to their nests (great mouse-nest material) to kill ticks. You can get them at hardware stores or from amazon.com. There is also information online on how to make your own, search for “how to make your own tick tubes.”

And, back in 2014, Maria Gomes-Solecki of the University of Tennessee developed a way to vaccinate mice against Lyme disease. A human vaccine for Lyme turned out to be too dangerous to use, but Gomes-Solecki developed an oral version of the vaccine that seems to work well in mice (less concern about the danger if it’s mice, too). And if you set out pellets of oatmeal with the vaccine for local mice, then the mice get immune to Lyme, and the ticks that suck their blood also get the mice’s Lyme antibodies that prevent Lyme disease.29 This has not (yet) been commercialized.
Changing suburban and rural landscaping to be less friendly to mice and ticks is recommended by the CDC. For example, getting rid of invasive Japanese barberry has been shown to decrease both mice and ticks. Japanese barberry primarily infests New England, the mid-Appalachian states, and the upper Midwest, the same places where Lyme disease is most prevalent.

**Lyme Vaccines**

We have safe, effective vaccines for many things: measles, mumps, whooping cough, tetanus, influenza... but not one for Lyme disease, at least for humans. There is a vaccine for dogs, and most veterinarians now strongly recommend it. Back in 1998, there was a FDA-approved vaccine for Lyme disease called LYMErix, but the manufacturer withdrew its product from the market amidst media coverage, fears of vaccine side-effects, and declining sales. Even though it appeared safe and effective; it was likely a victim of the then-rising anti-vaccine movement.

As of summer 2020, though, a human Lyme vaccine was shown to be effective in Phase 2 (of 3) trial and is expected to be available in 2024. A monoclonal antibody shot that can prevent Lyme disease for a year is also in development, and expected to be available in 2024.

**Clinical Lyme Disease**

In the 19th century, syphilis was known as *The Great Imitator*, but in 21st century North America, that title must go to Lyme disease. The incubation period ranges from days to years, and the manifestations are many and varied.

Early localized infection is characterized by *erythema migrans*, which used to be called *erythema chronica migrans* but it’s not really that chronic. This is a red, raised hive-like patch which, unlike hives, is *not* migratory and doesn’t go away with an epinephrine injection. It usually appears 3-30 days after the bite. A third of the time it has central clearing except a central red point or area (“target lesion”); see the picture of my daughter’s leg on the next page, the other two-thirds of the time it has no central clearing; half of the time it will be on the lower extremities or buttocks. The table provides more information about erythema migrans from a medical journal article.

About 10% of the time erythema migrans can develop vesicles or blisters, and it can sometimes be itchy as well as tender, making it easy to confuse with poison ivy dermatitis or ringworm. It tends to go away in about four weeks. A patch at the site of a tick bite should be >2 inches (5 cm) in diameter to be considered erythema migrans; smaller patches may be just a local allergic reaction to the tick bite.

About 80% of people with early localized Lyme disease will have erythema migrans. Which means it’s hard to tell that those other 20% have Lyme disease.

Some with erythema migrans will develop low-grade fever, malaise, and myalgias, but cold symptoms or vomiting and diarrhea are rare. Some with early Lyme Disease have similar systemic symptoms but no rash, which makes diagnosis quite difficult, especially because blood tests have many false positives (see below).

Early disseminated infection occurs when, days to weeks following the tick bite, the causative Rickettsial organism, *Borrelia burgdorferi*, spreads through the bloodstream to joints, heart, nervous system, and distant skin sites. This may occur without evidence of early localized infection.

Some people (a tenth to a quarter of those with a single lesion) will develop erythema migrans in areas away from the initial bite. These tend to be on the same extremity but may be anywhere; sometimes they are in places unusual for cellulitis or poison ivy (axilla, groin, popliteal fossa, back), which helps the diagnosis. The classic picture (next page) of multiple target lesions is of my daughter Laurel’s leg in 2005 when she was five years old, and the rash was misdiagnosed as hives by her pediatrician. The picture on this page is the more common and more ambiguous erythema migrans; note the red dot in the center.

Most people recover from early Lyme disease spontaneously. Late Lyme disease may occur after untreated erythema migrans or by infection with *B. burgdorferi* without erythema migrans. The distinction between early disseminated infection and late Lyme disease is still unclear, some classifying neurological or cardiac manifestations as one or the other. As we are concerned primarily with early Lyme disease, here is a high-level overview of this complex subject.
About half of those with erythema migrans have *B. burgdorferi* in their blood, and about half of those with untreated erythema migrans will go on to have arthritis, usually in a knee; one out of ten will have neurological symptoms, most commonly facial nerve palsy; and one out of twenty will have cardiac problems, most likely atrioventricular block. Treatment usually prevents these sequelae.32

**Lyme arthritis** is intermittent, usually in the knee or other large joints, but in about one out of ten, may become persistent. Due to presumed autoimmune mechanisms, this may persist after elimination of the spirochetes.33

**Neurological involvement** in late Lyme Disease comes in two main forms. Most common is involvement of a single nerve, often the facial nerve: Bell's Palsy.† There are recommendations to obtain blood tests in endemic areas.34 There are now recommendations to treat Bell's Palsy in Lyme-endemic areas and seasons (spring, summer and fall) for Lyme disease pending test results: “Patients with peripheral facial palsy who present during endemic seasons in geographic areas where Lyme disease incidence is high should be treated with empiric antibiotics while awaiting Lyme serology results.”35 Particularly in Pennsylvania, where about half of cases of Bell’s Palsy are thought to be from Lyme Disease (higher than anywhere except Switzerland),36 empiric treatment for Lyme Disease pending test results is becoming the standard of care. Bell's Palsy seems to follow acute Lyme Disease by about a month,38 so testing should be fairly reliable (see below); but as no test is 100% sensitive, there is still an argument for continuing to treat all cases of Bell's Palsy in Pennsylvania and perhaps other endemic states for Lyme Disease, regardless of test results, or to repeat the testing in 2-3 weeks if initially negative.39

If you do a lumbar puncture in a patient with Lyme facial palsy – which is recommended only if you suspect bacterial rather than Lyme meningitis – there is a high percentage who will have evidence of meningitis. However, there is an emerging consensus to patients Lyme meningitis with oral rather than IV antibiotics.37

Although it is common to treat Bell's Palsy with a course of steroids, this appears to be harmful if the cause is Lyme disease; if you are treating with oral antibiotics for Lyme disease, don't give steroids.37

Long-term follow-up of those with Lyme Bell’s Palsy shows excellent results from standard treatment.39

A percentage of untreated patients will have an indolent lymphocytic encephalo-meningitis (infection of the brain and spinal fluid), with a variety of neurological and psychological features. These symptoms tend to spontaneously resolve in weeks or months. However, up to 5% of untreated patients may go on to chronic neuroborreliosis (headache, sleep disturbance, other neurological symptoms),40 which can be treated by a month of IV ceftriaxone.41

**Cardiac involvement** in Lyme Disease is most commonly atrioventricular block (AV block, “heart block”) with a low heart rate, sometimes requiring a temporary pacemaker but seldom needing a permanent pacer. It may also present as acute myocarditis (acute inflammation of heart muscle). Those with acute Lyme myocarditis are at risk for sudden cardiac death.42 Chronic cardiomyopathy is rare in the US but has been reported in Europe.

**Chronic Lyme disease**, at least to a good approximation, does not exist. Some patients whose Lyme disease has been appropriately treated will have fatigue, musculoskeletal pain, difficulties with concentration and short-term memory, or some combination of these, which is classified as “post–Lyme disease symptoms,” and if longer than 6 months, “post–Lyme disease syndrome.”44 However, Seltzer et al found out that, if you follow those with acute Lyme Disease for a long time, there is no more chronic fatigue, fibromyalgia or similar chronic problems than with matched controls.45 Those who get recurrent erythema migrans after antibiotic treatment almost always have reinfection with a new strain of Lyme, not recurrence of the original infection.46

**Tests for Lyme disease**

**Most patients with early Lyme disease, particularly if B. burgdorferi is still localized to the skin, do not yet have a humoral immune response to the spirochete (detectable antibodies in the blood).** You have to diagnose erythema migrans when you recognize the characteristic appearance of the skin rash in persons who live in or have recently traveled to regions where Lyme disease is endemic.47

If you have a patient in the ED with what looks like erythema migrans, there is no point in sending any tests. Blood and skin biopsy cultures are only performed in research laboratories. You could send a blood test (serology) performed as a baseline, but you and your patient need to know that prompt treatment with an antibiotic (which is the standard of care) may prevent the serology from turning positive. If you clinically diagnose a patient with erythema migrans and treat appropriately, subsequent negative serological tests do not mean that you misdiagnosed the patient, but more likely that you acted in time to prevent a detectable immune response.48 As a 2020 clinical guideline by the Infectious Disease Society of America says:

**In patients with potential tick exposure in a Lyme disease endemic area who have 1 or more skin lesions compatible**

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† https://en.wikipedia.org/wiki/Bell%27s_palsy
‡ https://en.wikipedia.org/wiki/Neuroborreliosis
32 https://en.wikipedia.org/wiki/Atrioventricular_block
33 https://en.wikipedia.org/wiki/Neuroborreliosis
34 https://en.wikipedia.org/wiki/Bell%27s_palsy
35 https://en.wikipedia.org/wiki/Neuroborreliosis
36 https://en.wikipedia.org/wiki/Erythema_migrans
37 https://en.wikipedia.org/wiki/Bell%27s_palsy
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48 https://en.wikipedia.org/wiki/Neuroborreliosis
with erythema migrans, we recommend clinical diagnosis rather than laboratory testing (strong recommendation, moderate quality evidence). In patients with 1 or more skin lesions suggestive of, but atypical for erythema migrans, we suggest antibody testing performed on an acute-phase serum sample (followed by a convalescent-phase serum sample if the initial result is negative) rather than currently available direct detection methods such as polymerase chain reaction (PCR) or culture performed on blood or skin samples (weak recommendation, low-quality evidence). If needed, the convalescent-phase serum sample should be collected at least 2–3 weeks after collection of the acute-phase serum sample.

Translated into simple English: if it doesn't look like erythema migrans, but just possibly might be, send the blood test, and if it's negative, make sure that you get a repeat test 2-3 weeks later to make sure you haven't missed it. (That's problematic when, as in the ED, follow-up is not assured. It makes more sense, especially since some of these skin rashes may be cellulitis, and doxycycline is good for cellulitis, to treat with doxycycline and not test.)

This same IDSA guideline recommends Lyme testing for those with:

- In patients presenting with 1 or more of the following acute disorders: meningitis, painful radiculoneuritis, mononeuropathy multiplex including confluent mononeuropathy multiplex, acute cranial neuropathies (particularly VII, VIII, less commonly III, V, VI and others), or in patients with evidence of spinal cord (or rarely brain) inflammation, the former particularly in association with painful radiculitis involving related spinal cord segments, and with epidemiologically plausible exposure to ticks infected with B burgdorferi, we recommend testing for Lyme disease (strong recommendation, moderate-quality evidence).

The IDSA recommends against Lyme testing for:

- In patients with typical amyotrophic lateral sclerosis, relapsing-remitting multiple sclerosis, Parkinson's disease, dementia or cognitive decline, or new-onset seizures, we recommend against routine testing for Lyme disease (strong recommendation, moderate-quality evidence).

The IDSA recommends against Lyme testing for:

- In patients with typical amyotrophic lateral sclerosis, relapsing-remitting multiple sclerosis, Parkinson's disease, dementia or cognitive decline, or new-onset seizures, we recommend against routine testing for Lyme disease (strong recommendation, moderate-quality evidence).

- In patients with neurological...
syndromes other than those listed in [the bullet above and the one above that] in the absence of a history of other clinical or epidemiologic support for the diagnosis of Lyme disease, we recommend against screening for Lyme disease (strong recommendation, low-quality evidence).

- In patients presenting with nonspecific magnetic resonance imaging (MRI) white matter abnormalities confined to the brain in the absence of a history of other clinical or epidemiologic support for the diagnosis of Lyme disease, we suggest against testing for Lyme disease (weak recommendation, low-quality evidence).

- In patients with psychiatric illness, we recommend against routine testing for Lyme disease (strong recommendation, low-quality evidence).

- In children presenting with developmental, behavioral or psychiatric disorders, we suggest against routinely testing for Lyme disease (weak recommendation, low-quality evidence).

If you are charged with talking with a patient for whom one of your partners sent a Lyme titre for probable acute Lyme disease, choose your words carefully. “The test was negative, which shows that you didn't have untreated Lyme disease prior to about a month ago.” “What use is the test, then? Why did he/she send it?” “Maybe as a baseline test to see if you have a positive test from a prior episode of Lyme disease that you might not have recognized at the time.” For other possible manifestations of Lyme disease (carditis, neuritis, new heart block), admit or discharge for outpatient workup as seems appropriate. In such cases, it may be appropriate to send a Lyme test from the ED to aid the admitting physician or follow-up physician.

Guidelines established by the Association of State and Territorial Public Health Laboratory Directors and the U.S. Centers for Disease Control and Prevention (CDC) recommend the use of a two-test protocol for the serologic diagnosis of Lyme disease. First is a sensitive but nonspecific screening test. If the screening test is positive, then follows specific immunoglobulin M (IgM) and/or IgG immunoblotting (IB), depending on the date of disease onset. The test to order is, depending on which lab it goes to, something like Lyme Disease Antibodies, Including Reflex to Western Blot on Positive.

DNA tests (PCR=polymerase chain reaction) are also available, but not useful, as fragments of dead bacterial DNA may linger long (months, maybe years) after successful treatment, and DNA PCR misses half of acute cases. DNA tests of ticks for Lyme disease are also useless. The large urgent care chain MedExpress refuses to send ticks for testing, as insurance won't pay for such useless tests; people who really want to test their ticks are referred to labs that charge money ($50-$250; search online) up front for the testing. The CDC says:

- If the test shows that the tick contained disease-causing organisms, that does not necessarily mean that you have been infected.

- If you have been infected, you will probably develop symptoms before results of the tick test are available. You should not wait for tick testing results before beginning appropriate treatment.

- Negative results can lead to false assurance. For example, you may have been unknowingly bitten by a different tick that was infected.

One problem with Lyme disease testing is that many people have had Lyme disease in the past without knowing it, have recovered without sequelae, and even 10-20 years later, some will have positive IgM as well as IgG titres with no actual infective symptoms due to Borrelia.

Another problem is that people in areas with no significant Lyme disease with chronic fatigue, chronic pain or similar complaints get a Lyme titre done. Given such a low likelihood of Lyme in this situation especially if someone's in an area without Lyme disease, and even with a very accurate test, the vast majority of positive tests will be false positives, and the patient doesn't actually have Lyme disease. And, unfortunately, millions and millions of Lyme disease tests are done every year. Yet another problem is that there are cases of what look, for all the world, just like Lyme disease, particularly in the southeast states and the Caribbean, but serologic tests are negative, making an as-yet-discovered Borrelia likely. At least a portion of this Lyme variant is vectored by the lone star tick, Amblyomma americanum, and has been named southern tick-associated rash illness (STARI) or Masters’ disease after the physician who first reported it. One causative organism, Borrelia lonestari, has been cultured, and the infection appears to respond to doxycycline. Over the past two decades, the lone star tick has spread into the center of the USA and even into New England.

One final note on testing (though you can certainly find much, much more in the medical literature on testing for Lyme): IgM vs IgG antibodies. The traditional teaching is that, when you get infected with something, IgM antibodies pop up in your blood right away after an infection, in a week or two and then gradually go away, and that IgG antibodies develop later and hang around providing you some ongoing immunity. But with Lyme disease, even IgM antibodies can stay high for a long time, even though you are perfectly healthy. Nobody knows why.

**Treatment**

**In vivo (human/animal) testing confirms** that B. burgdorferi is sensitive to oral antibiotics, listed in decreasing order of preference:

- doxycycline,
- amoxicillin,
- cefuroxime axetil (e.g., Ceftin) and
- azithromycin (e.g., Zithromax).

IV ceftriaxone (e.g., Rocephin) is highly effective and appropriate for more severe cases. With moderate cases, for instance with a significant fever but not toxic-appearing, I give a single dose of IV ceftriaxone  2 g and then send the patient home on oral doxycycline.

Pediatricians and pharmacologists are getting increasing nonchalant about prescribing doxycycline to kids and pregnant
The standard treatments for erythema migrans, or early disseminated Lyme disease, including facial nerve palsy, mild arthritis or carditis (a PR interval of less than 0.3 second), include doxycycline 100 mg PO BID, amoxicillin 500 mg PO TID, or cefuroxime axetil (e.g., Cefin) 500 mg PO BID, or equivalent pediatric doses, for 14-21 days; longer courses seem appropriate for those with more severe disease. There is evidence that a 10-day course of doxycycline is as good as a 20-day course at least for erythema migrans. Doxycycline is best in that it also covers anaplasmosis, which can be transmitted by the same ticks that transmit Lyme disease and STARI/Master’s disease.

Lyme arthritis is usually in a single joint, often the knee, which is warm and swollen, but not so much as a joint that is septic with, say, Staphylococcus aureus. It may occur a couple of years after the initial infection, but there are documented cases of it occurring only four days after erythema migrans. In such a case, initial blood tests would likely be negative, but it’s still worth sending them. However, there are recommendations to treat arthritis with a longer (30-day) course of oral antibiotic instead of the shorter (14 or perhaps 10-day) course for simple erythema migrans. An unanswered question is the initial treatment of a new-onset inflammatory knee arthritis (one that does not appear septic) in endemic areas. Neither blood tests nor tests of a knee fluid aspiration are necessarily diagnostic. In this instance, the internal medicine paradigm of starting treatment only after achieving a diagnosis might be inferior to the emergency medicine paradigm of starting treatment presumptively; perhaps the benefits of earlier antibiotic treatment outweigh the harms of a few days of an antibiotic, at least in endemic areas. You could start antibiotic treatment and send the usual tests for inflammatory arthritis such as lupus and rheumatoid arthritis and discharge from the ED. The follow-up physician could stop the antibiotics if another cause of the inflammatory arthritis becomes apparent. The IDSA 2020 guidelines for Lyme disease state:

When assessing possible Lyme arthritis, we recommend serum antibody testing over PCR or culture of blood or synovial fluid/tissue (strong recommendation, moderate quality of evidence). In seropositive patients for whom the diagnosis of Lyme arthritis is being considered but treatment decisions require more definitive information, we recommend PCR applied to synovial fluid or tissue rather than Borrelia culture of those samples (strong recommendation, moderate quality of evidence).

For patients with Lyme arthritis, we recommend using oral antibiotic therapy for 28 days (strong recommendation, moderate-quality evidence).

In patients with Lyme arthritis with partial response (mild residual joint swelling) after a first course of oral antibiotic, we make no recommendation for a second course of antibiotic versus observation (no recommendation, knowledge gap). Consideration should be given to exclusion of other causes of joint swelling than Lyme arthritis, medication adherence, duration of arthritis prior to initial treatment, degree of synovial proliferation versus joint swelling, patient preferences, and cost. A second course of oral antibiotics for up to 1 month may be a reasonable alternative for patients in whom synovial proliferation is modest compared to joint swelling and for those who prefer repeating a course of oral
antibiotics before considering IV therapy.

In patients with Lyme arthritis with no or minimal response (moderate to severe joint swelling with minimal reduction of the joint effusion) to an initial course of oral antibiotic, we suggest a 2- to 4-week course of IV ceftriaxone over a second course of oral antibiotics (weak recommendation, low-quality evidence).

In patients who have failed one course of oral antibiotics and one course of IV antibiotics, we suggest a referral to a rheumatologist or other trained specialist for consideration of the use of disease modifying anti-rheumatic drugs (DMARDs), biologic agents, intraarticular steroids, or arthroscopic synovectomy (weak recommendation, very low-quality evidence). Antibiotic therapy for longer than 8 weeks is not expected to provide additional benefit to patients with persistent arthritis if that treatment has included 1 course of IV therapy.

The annual incidence of Lyme disease overall in endemic areas is about 100-200 per 100,000. A third of reported cases are, or include, arthritis. That means an incidence, again in endemic area, of 30-60/100,000. But the CDC suspect that only a tenth of cases are actually reported. That brings us to an estimated incidence of Lyme arthritis of 300-600/100,000 in endemic areas. The incidence for rheumatoid arthritis, probably the most common non-Lyme inflammatory arthritis, is only about 60/100,000 in Ontario, Canada. Similarly, the incidence in one county in Minnesota is similar about 50-60/100,000. This suggests that, in Lyme-endemic areas, Lyme arthritis is probably a more common cause of new-onset inflammatory arthritis than rheumatoid arthritis, lupus or less-common rheumatic conditions, making early empiric antibiotic treatment pending test results more attractive.

Doxycycline should be avoided in pregnant women. The other problem I have with doxycycline is that I see they people with erythema migrans right before a summer vacation at the beach, and doxycycline is known to cause photosensitivity. I explain to patients to whom I prescribe doxycycline: “It makes you much easier to get sunburned.”

An important note: if you aren’t sure if what you see is cellulitis or erythema migrans, do not treat solely with cephalaxin (e.g., Kellex) or trimethoprim-sulfamethoxazole (e.g., Bactrim); they are not effective against B. burgdorferi. So if you see “cellulitis” that’s not improving with one of these antibiotics, consider treating for erythema migrans, particularly doxycycline, which is pretty good for cellulitis, too.

More serious central nervous system disease (e.g., meningitis, encephalitis), peripheral or cranial neuropathy, or more serious arthritis or carditis, including those with a PR interval of greater than 0.5 second, are treated with ceftriaxone 2 g IV daily, cefotaxime 2 g IV Q8H, or high-dose penicillin G 18-24 million units IV daily either continuous or divided Q4H, also for 14-21 days.

One author recommends that any pregnant patient with any Lyme disease should be treated with 2 g of ceftriaxone IV daily for 14 days.

The IDSA 2020 guidelines recommend admission for those with Lyme involvement of the heart:

In patients with or at risk for severe cardiac complications of Lyme disease including those with significant PR prolongation (PR > 300 milliseconds), other arrhythmias, or clinical manifestations of myopericarditis, we recommend hospital admission with continuous ECG monitoring (strong recommendation, very low-quality evidence). Clinical manifestations of Lyme carditis include exercise intolerance, palpitations, presyncope, syncope, pericarditic pain, evidence of pericardial effusion, elevated biomarkers (such as troponin), edema, and shortness of breath.

LYME CONTOVERSY AND QUACKERY (ESPECIALLY IN PENNSYLVANIA)

Lyme disease is controversial. Don’t worry, the diagnosis and treatment of acute Lyme disease in the ED is quite straightforward, but “chronic Lyme disease” is a whole different can of worms. The National Institutes of Health recommend against the term “chronic Lyme disease” and recommend we talk about “post-treatment Lyme disease syndrome (PTLDS).” Why? Because there are many people who are convinced, against all evidence, that their [pick one: a. chronic fatigue b. fibromyalgia c. memory loss] is “chronic Lyme disease.” And, according to Cooper, writing in the Pediatric Infectious Disease Journal in 2004, the Internet is a vast wasteland of Lyme disease misinformation. There are organizations devoted to what seems now a sort of religious cause, such as the International Lyme and Associated Diseases Society. Let me tell you a story, though I can’t tell you where I heard this, if I did, I’d have to shoot you (just kidding). John Foster Dulles used to be the US Secretary of State. He had some usually well-controlled psychiatric issues, but at one point, had to be hospitalized due to paranoid delusions that the Israeli secret service (the Mossad) was surveilling and harassing him. The psychiatrist treating him found his problem very difficult to treat, as the Mossad really was surveilling and harassing him. Similarly, there is some evidence that B. burgdorferi might hide and then erupt later, though others think this may be autoimmune without actual infection. B. burgdorferi has some tricks to prevent clearance by the immune system, which may result in persistent infection, variously called round bodies, persisters, or biofilm forms. In untreated patients, cultures...
It is also likely that Lyme disease can trigger a variety of autoimmune problems, which persist after the elimination of all spirochetes, at least in the case of Lyme arthritis. Standard regimes of doxycycline, amoxicillin or ceftriaxone usually eliminate the acute disease, and longer courses of treatment with these standard antibiotics does not improve symptoms. Though still controversial, there is some suspicion that some patients may have persistent forms, and finding combinations of antibiotics to eliminate these persistent forms are active areas of research.

Infectious disease specialists tend to treat such recurrences with a longer course of antibiotics, usually doxycycline, but for less than four weeks. Though still controversial, there is some suspicion that some patients may have persistent forms, and finding combinations of antibiotics to eliminate these persistent forms are active areas of research.

In 2005, concerns about inappropriate laboratory testing prompted the CDC and FDA to issue a warning about commercial laboratories that conduct testing for Lyme disease by using assays whose accuracy and clinical usefulness have not been adequately established. These tests include urine antigen tests, immunofluorescent staining for cell wall-deficient forms of Borrelia burgdorferi, and lymphocyte transformation tests. Some laboratories perform polymerase chain reaction tests for B. burgdorferi DNA on inappropriate specimens such as blood and urine or interpret Western blots using criteria that have not been validated and published in peer-reviewed scientific literature.

Sigal writes: The diagnosis should be based on symptoms and the probability of exposure to the Lyme spirochete. Laboratory evaluation is appropriate for patients who have arthritic, neurologic, or cardiac symptoms associated with Lyme disease, but it is not appropriate in patients who have nonspecific symptoms, such as those of chronic fatigue syndrome or fibromyalgia.

A great variety of treatments, including outright quackery and malpractice, have evolved for the treatment of self-diagnosed "chronic Lyme disease," often without a history of positive Lyme serology. These include but are not limited to the following useless and, in some cases, very dangerous "therapies":

- Colloidal silver.
- Intracellular hyperthermia therapy (ICHT): taking 2,4-dinitrophenol (DNP) to "rev up mitochondria" and cause intracellular hyperthermia, despite the fact that DNP, when tried as a diet medication back in the 1930s, killed people.
- Rife machines (electromagnetic devices that "sync their frequencies" to the spirochetes).
- Hydrogen peroxide injections.
- Intravenous ozone, which has been reported to cause myocardial infarction ("heart attack").
- Infecting oneself with malaria.

* https://www.niaid.nih.gov/diseases-conditions/lyme-disease-antibiotic-treatment-research
A less overtly quackish treatment is prolonged treatment with antibiotics, particularly IV ceftriaxone, which has resulted in biliary problems including likely iatrogenic cholecystitis leading to cholecystectomy.\footnote{30} One 30 year old woman died from an infected IV that had been in place for two years, for treatment of unsubstantiated Lyme disease.\footnote{30} In June 2017, the CDC’s MMWR (Morbidity and Mortality Weekly Report) featured a nice review of the literature, and related some cases studies related to long-term antibiotics for “chronic Lyme disease”: 92

- An adolescent girl with chronic fatigue syndrome saw a “Lyme-literate doctor” and received a diagnosis of chronic Lyme disease. This doctor gave her 3 months of oral antibiotics, and then when that didn’t work, ordered her a PICC line (“peripherally inserted central catheter”; long term indwelling IV catheter) and then two months of IV antibiotics. After the IV antibiotics were done, the doctor neglected to have her PICC line removed, and she got septic (bloodstream infection) from the PICC line, with fever and low blood pressure and had to be rushed to the Emergency Department, resuscitated, and then admitted to the Intensive Care Unit. After a complicated several-week stay in the hospital, she was eventually discharged home.

- A woman in her 40s developed a flu-like illness, with joint and muscle pains. A year later, based on a positive Lyme titre (properly done, but indicating only that she’d been exposed to Lyme disease sometime prior to the test being done), she was treated with two 4-week courses of oral doxycycline. Later, she developed fatigue, cognitive difficulties, and poor exercise tolerance, and two years after her initial diagnosis, a “Lyme-literate doctor” diagnosed her with chronic Lyme disease and treated her with IM (intramuscular) penicillin for 5 weeks, and when that didn’t work, with IV antibiotics for 10 months via a port (a surgically inserted catheter that leads from a major vein in the chest to a subcutaneous site that provides easy IV access). A year later, she got a new port, and four weeks more of IV antibiotics. She ended up getting back pain, shortness of breath, and malaise, and was admitted to the hospital where she was found to have a bloodstream \textit{Pseudomonas} infection in her spine.

- A woman in her 50s got weakness, swelling, and tingling in her extremities and was diagnosed with inflammatory demyelinating polyneuropathy and later amyotrophic lateral sclerosis (ALS, “Lou Gehrig’s disease”). She saw a a “Lyme-literate doctor” who diagnosed her with chronic Lyme disease, babesiosis, and Rocky Mountain spotted fever, and, after homeopathic remedies and herbs didn’t help, IV antibiotics. After seven (7) months, her pain was a bit better, but the weakness was worse. From the antibiotics, she developed \textit{C difficile} enterocolitis that caused severe abdominal cramps and diarrhea that lasted more than two years and ended up dying of ALS.

- A woman in her 30s with joint pain was given a diagnosis of “chronic Lyme disease” (along with babesiosis and Bartonella infection) by a “Lyme-literate doctor.” She had a PICC for long-term antibiotics, got 3 weeks of antibiotics, and then got septic and died.

Some people with fibromyalgia or chronic fatigue and positive Lyme titers (or even without such titers) are so desperate for antibiotics that, when they can’t find doctors to prescribe them, as per reports in the popular press (see \url{quackwatch.org}) they resort to veterinary antibiotics. Some of these antibiotic-seekers are quite politically active, and they have such a hard time finding doctors to prescribe their antibiotics (LLMDs or “Lyme-Literate MDs”). In 2011 they introduced a bill into the Pennsylvania Senate that would ensure insurance coverage for prolonged courses of antibiotics and prevent any misconduct hearings or actions by the Board of Medicine against those accused of inappropriately prescribing prolonged antibiotics for presumed Lyme disease. Some LLMDs are treating problems such as autism, multiple sclerosis and amyotrophic lateral sclerosis with long-term antibiotics on the assumption that they are really forms of Lyme disease. And the chief of rheumatology at Tufts has been harassed, stalked, and threatened by patients and patient advocacy groups demanding that he endorse long-term antibiotic treatment for “chronic Lyme disease” – to the point where he had to be assigned security guards.\footnote{93} There have been many media “exposés” of how mainstream doctors are ignoring the needs of “chronic Lyme disease” patients for prolonged antibiotics, so the public perception seems to align, not with mainstream medicine, but more with the quacks.\footnote{40} In late 2014, the Pennsylvania legislature passed, and the Governor signed, a Lyme Disease law that provides for tick surveillance and education, but omitted any special provisions protecting quackery. The chances of any new Lyme quack-protection bill in Pennsylvania seem remote.

Lightfoot et al concluded that for most patients with a positive Lyme antibody titer and only symptoms of fatigue or nonspecific muscle pains, the risks and costs of intravenous antibiotic therapy exceed the benefits. \textit{In areas endemic for Lyme disease, the incidence of false-positive serologic results in patients with nonspecific myalgia or fatigue exceeds by four to \textit{one the incidence of true-positive results}...} And Klemperer showed, in placebo-controlled trials, that such patients do not benefit from ninety days of antibiotics.\footnote{95} \url{Quackwatch.org} gives the following bullets as their bottom line, which I heartily endorse:

- Lyme disease, when diagnosed early, is readily treatable with oral antibiotics.
- Positive antibody tests, by themselves, do not provide a sufficient basis for diagnosing Lyme disease. The diagnosis should be based on the overall clinical picture, including medical history and physical findings.
- Negative antibody testing after the first few weeks strongly suggests that the patient does not have Lyme disease.
- Many patients with chronic, nonspecific symptoms (such as headaches, fatigue, muscle aches, mental confusion, or sleep disturbances) mistakenly believe they have Lyme disease.
- Intravenous antibiotic therapy, when given appropriately, should not last more than a month. It should not be given unless oral antibiotic therapy has failed, and persistent active infection has been demonstrated by culture, biopsy, or other bacteriologic technique.
- Malaria therapy, intracellular hyperthermia therapy, hyperbaric oxygen therapy, colloidal silver, dietary supplements, and herbs are not appropriate measures for treating Lyme disease. Doctors who recommend them should be avoided.
Disinformation on “CHRONIC LYME DISEASE!!!!!” is so widespread (I wonder if the Russians had a hand in it?) that some suggest that medical professionals dump the tainted term “Lyme disease” and speak about “Lyme borreliosis” (LB) or B. burgdorferi sensu lato infection (Bbsl infection).86

My bottom line: if a patient presents to the ED with likely or even possible erythema migrans, or likely or possible early disseminated Lyme Disease, I treat with a short course of antibiotics. If someone presents something such as inflammatory arthritis, neuropathy, or cardiac conduction defects at an early age, and I’m suspicious of late Lyme disease (which, as I work in an endemic area, I sometimes have to be), or probable recurrent Lyme disease, I consult an ID specialist (infectious diseases) who is knowledgeable about Lyme disease, send a titre unless they’ve had a positive one in the past, start on the antibiotic the ID specialist recommends (usually doxycycline), and have them follow up with the ID doc or the PCP in the office in a week or so.

If I see someone thinking that they have chronic Lyme disease, I refer to a reputable PCP or infectious disease specialist without ordering any sort of testing and without ordering any antibiotics. I suspect PCP or ID specialist will not thank me for this referral.

Other Tick-Associated Diseases

Anaplasmosis

The same Ixodes ticks that transmit B. burgdorferi may be infected with and transmit Anaplasma phagocytophila (previously referred to as Ehrlichia phagocytophilum), which causes human granulocytic anaplasmosis (previously called ehrlichiosis). In the upper Midwest (Wisconsin) about one in ten of patients with early Lyme disease will also have anaplasmosis, but it’s not as frequent in New England. The treatment of choice is doxycycline, and there are strong recommendations for empiric treatment pending the results of PCR testing.87,88

Babesiosis

I. scapularis ticks may also carry the malaria-like Babesia microti, which causes babesiosis (“malaria of the Northeast” “Montauk Malaria”). The disease is most common in coastal southern New England, particularly eastern Long Island (Montauk is the town at the far east end of Long Island), Fire Island, Nantucket Island and Martha’s Vineyard. In these areas, about one in ten patients with Lyme disease also have babesiosis. Babesiosis has been reported in other areas of New England and the northern midwest.

Clinical clues to babesiosis (or early Lyme disease complicated by babesiosis) include an unusual severity of symptoms, including fatigue, headache, sweats, chills, anorexia (loss of appetite), emotional lability, nausea, conjunctivitis, splenomegaly (enlarged spleen), elevated liver enzymes, and hemolytic anemia as well as thrombocytopenia (low platelets). Babesiosis is diagnosed primarily by repeated thick and thin Giemsa smears, just like malaria.49 A history of a blood transfusion or travel to the endemic area within the past nine weeks combined with the above history should raise suspicion of babesiosis.

Babesiosis is treated with atovaquone and azithromycin.49 The 2020 IDSA Lyme guidelines state:

In patients with Lyme disease who have a high-grade fever or characteristic laboratory abnormalities, clinicians should assess for possible coinfection with Anaplasma phagocytophilum and/or B. microti infection in geographic regions where these infections are endemic (good practice statement).

Coinfection should be investigated in patients who have a persistent fever for >1 day while on antibiotic treatment for Lyme disease. If fever persists despite treatment with doxycycline, B. microti infection is an important consideration. Characteristic laboratory abnormalities found in both anaplasmosis and babesiosis include thrombocytopenia, leukopenia, neutropenia, and/or anemia. Evidence of hemolysis, such as elevated indirect bilirubin level, anemia, and elevated lactate dehydrogenase are particularly suggestive of babesiosis.

Borrelia miyamotoi disease (BMD)

Some people develop a fever without the usual symptoms and signs of other bacterial or viral illnesses. Tickborne or mosquito-borne infections are a reasonable suspicion; mosquito-borne viral infections, such as West Nile virus, have no specific treatment. But more and more tickborne diseases are being found, and many of them respond to doxycycline, just like Lyme disease and anaplasmosis (ehrlichiosis). Borrelia miyamotoi disease (BMD) was identified in Russia in 2011 and in New England in 2013. It may cause fever, severe headache, elevated liver enzymes, low white blood cell count, and low platelets. In a survey of blood sent for testing for tickborne diseases in New England, about 10% were positive for BMD. A survey of New England ticks showed that 1-5% are infected with Borrelia miyamotoi. No test to guide urgent treatment is available. BMD seems to respond to doxycycline, amoxicillin and ceftriaxone, so treatment is the same as Lyme disease.100

At this rate, we will find a new doxycycline-responsive tick-borne disease every 5-10 years. This convinces me that in areas and seasons where and when tickborne diseases are common (e.g., Pennsylvania in the spring, summer and to a lesser extent fall), we should treat people with unexplained fevers with doxycycline.

Rocky Mountain Spotted Fever

Rocky Mountain Spotted Fever (RMSF) is a misnomer, it’s actually common in the eastern US than in the Rocky Mountains. It’s caused by Rickettsia rickettsii, and transmitted by a variety of ticks, most commonly the dog tick. Classic early symptoms include fever, nausea and vomiting, so are quite nonspecific. Later symptoms often include abdominal pain and diarrhea and arthralgias. Between 2008 and 2012, the number
of reported cases increased 8-fold, but the disease seemed to become milder. The explanation may be the Lone Star Tick expanding its range northward, paralleling the expanding deer population. This tick carries *Rickettsia amblyomnii*, which is closely related to *R. rickettsii* and might test positive on tests for *R. rickettsii*. However, *R. amblyomnii* doesn’t seem to cause significant disease in humans. Some think that if you get infected with *R. amblyomnii* it might act just like a vaccine, making you create antibodies that protect you against *R. rickettsii* and RMSF.\footnote{101}

The maculopapular and later petechial rash of Rocky Mountain spotted fever doesn’t usually appear until days 2-5, and it occurs in only one-third to two-thirds of patients with RMSF. In half to two-thirds of those with a rash it appears on the palms and soles and then moves toward the torso. Moral: don’t depend on a rash for your diagnosis.

The diagnosis of RMSF is clinical, not based on lab tests. That said, those who are seriously ill with RMSF usually have a normal WBC count, low platelets, low RBC count, elevated liver enzymes, elevated bilirubin and a low sodium. RMSF used to kill 30% and it’s still kills \textasciitilde{} 20%.\footnote{102} And, only about one in ten have the classic combination of fever, rash (classically a papular blanching rash on the hands and feet then spreading to the torso) and history of tick exposure. Treat based on suspicion, with either doxycycline or chloramphenicol.\footnote{103-105}\textasciitilde{}\textasciitilde{}\textasciitilde{}
The American Academy of Pediatrics says to use doxycycline for presumed RMSF or anaplasmosis infection in children of any age.\footnote{106}

**Rare Weird Things: Tick Paralysis and Alpha-gal allergy**

Tick paralysis is caused by a neurotoxin secreted in the saliva of certain ticks and is a well-known cause of illness death in livestock and pets. In North America, tick paralysis is caused by the Rocky Mountain wood tick (*Dermacentor andersoni*) and the American dog tick (*Dermacentor variabilis*). Tick paralysis mimics, and is often mistaken for, Guillain-Barre syndrome: an ascending paralysis that is fatal in about one out of ten cases — yet quickly curable by simply detecting and removing the tick. It is likely that it is only caused by engorged and egg-laden female ticks. Other than the effects it causes, and that it is usually secreted from days 5-7 after attachment, little is known about the toxin. The tick is usually found on the scalp, and during the months April to June, when ticks are feeding.\footnote{107}

The saliva of *Amblyomma americanum*, the lone star tick, is known to cause hives or even anaphylactic allergy to a component of red meat (“alpha-gal”) in some who are bitten.\footnote{108} Some people also become allergic to ice cream from the bite of this tick. The range of the lone star tick is increasing, and estimates are that in 2018 there were 5000 cases of alpha-gal allergy in the USA. So if you like steak and ice cream, use a good insect repellent and treat your socks with permethrin.

One final weird thing which might or might not be caused by a tick bite. I am putting it in here in the hopes that someone might recognize it and tell me what it was. Multiple infectious disease docs I have asked have never heard of anything like it. When I was in the fourth grade, one sunny summer day, I was walking through a field of knee-high grass near my home, when I felt a sudden severe sharp pain on my right ankle, which lasted for maybe an hour. Looked there, didn’t see any insect or any rash. But a couple hours later, I developed a red bump on the ankle. It rapidly started spreading outwards, clearing in the center. It became a red circle just like you had it might act like a vaccine, making you create antibodies that protect you against *R. rickettsii* and RMSF.\footnote{101}

Ulceroglandular Tularemia

Once upon a time, on a hot summer day, I was involved in a wilderness search and rescue operation near Charlottesville, Virginia. After a successful operation, some of us adjourned to Lord Hardwicke’s Steakhouse. While sitting at the table, I noticed a stinging sensation on my right scalp. I reached up and scratched the area, and my finger came back with a small amount of pus on it. I went to the bathroom and washed my hands, and in the mirror some swelling of the back right side of my neck, and then felt my neck and could feel some warm, swollen lymph nodes. I took some Duricef (a cephalosporin antibiotic) that I had with me.

The area on my scalp quickly healed, but for the next couple of days the lymph nodes in my neck stayed swollen and warm and tender. I consulted one of my partners who suggested I try a different antibiotic, so I tried clindamycin. A few days later it was obvious that the clinda wasn’t working, so I curbside-consulted (asked him when he was in the ED to see a patient) one of the ENTs, he just suggested the antibiotic Bactrim, which didn’t work either.

As I was typing up a Wilderness EMT curriculum section on ulceroglandular tularemia, a bacterial infection carried by rabbits and occasionally transmitted to humans by the bite of an infected tick (or maybe mosquitoes, biting black flies or fleas). And it presents just like what happened to me, and doesn’t respond to most antibiotics, but does respond to doxycycline. I gave myself a dope-slap on the head, reached into my closet and grabbed some doxycycline that was there, and in a few days all my symptoms were gone; two weeks of doxy is recommended.