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 meningocephhalitis, Colorado tick fever, babesiosis, anaplasmosis (ehrlichiosis), and rarer diseases including Crimean-Congo hemorrhagic fever, cytaxozoonosis, 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.

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 very similar black-legged tick species in northern California and Oregon, *Ixodes* *pacificus,* also transmits Lyme disease. 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.

*Amblyomma americanum,* the lone star tick, which transmits STARI or Master’s disease (very similar to Lyme Disease, see below), is found in the southern US.

PREVENTING TICK ATTACHMENT

Assuming you don’t want to wear a flea and tick collar, which doesn’t work that 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 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).

DEET is the most famous, and highly effective, but it 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 (known outside the US as icaridin or KBR3023, tradename Bayrepel) is marketed as Cutter Skinsations Ultra Light, Natrapel, Avon...
Skin so Soft Bug Guard Plus and Sawyer Premium 20% Picaridin. It 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’s important to choose a preparation with a vehicle that allows it to persist on the skin; the Cutter preparation lasts only 4.5 hours, whereas Natrapel lasts for about 8 hours and Sawyer Premium 20% Picaridin lasts 10-12 hours. It is about the same as DEET for protection against ticks. In one study of anopholes 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.7 Repel is oil of lemon eucalyptus, found in the leaves of the Eucalyptus citriodora although chemically synthesized, and, quite unlike other essentially-useless “herbal” repellents like Burt’s Bees All Natural Herbal and Bite Blocker Xtreme (organic), is virtually as effective as DEET. But it is very smelly.

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 legends), it turned out to be quite false. Consumer Reports tested Skin So Soft and found it ineffective (Consumer Reports, Volume 58, No. 7, July, 1993, pages 451 - 454), as did a study by Fradin1 (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, 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.8 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 an Avon Skin So Soft Bug Guard Plus IR3535 Expedition SPF 30 which, in addition to 20% IR3535 includes sunblock, a bad combination according to the CDC and Consumer Reports, because insect repellent should be applied sparingly (due to potential toxicity) and sunscreen should be applied liberally and frequently. DEET, as long as 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: Consumer Reports tested and rated these as follows (higher scores better):
96 Sawyer Fisherman's/Premium 20% Picaridin
87 Repel Lemon Eucalyptus
81 Natrapel 8 Hour (20% Picaridin)
74 Off! Deepwoods VIII (25% DEET)
69 Coleman SkinSmart (20% IR3535)

Cutter Skinsations, Cutter Natural, Burt's Bees, Babyganics Natural, Bull Frog Mosquito Coast, All Terrain kids Herbal Armor, California Baby Natural Bug Blend, Off! FamilyCare Clean Feel, and EcoSmart Organic all got scores of 33 or less. The Sawyer product provided 8.5 hours of protection against deer ticks in their tests; it has been renamed Sawyer Premium Insect Repellent 20% Picaridin.

The EcoSmart Organic provided only 1.3 hours. In 2016, The Medical Letter published a summary of available medical literature about insect repellents.11 It’s also possible to treat clothing with the “repellent” permethrin, though it doesn’t repel ticks, it kills them. 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’s highly effective, especially if you treat your socks, as ticks climb up your legs from the ground.12 I treated pairs of socks this way, but not my outdoor pants, as you have to remove any DWR (durable water-repellent) treatments before they can bond the permethrin to your clothing.

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, 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, so 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, but based on small human studies. There are a variety of devices for tick removal. 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. I’ve used it 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 better as it’s easier to grip, 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 Bandaid. 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, 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. According to the CDC, Lyme disease was the 6th most common Nationally Notifiable disease in 2008, and the most common tick-borne disease in the northern hemisphere. The big state of Pennsylvania has the most reported cases (>12,000 in 2016, 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% of southwestern PA nymphal blacklegged ticks are infected.

A variant of Lyme disease with different characteristics and caused mostly by *Borrelia afzelii* occurs in Europe and Scandinavia. There, erythema migrans 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.
Lyme Ecology

There is discord between hunting and animal rights groups about the role of deer culling in controlling Lyme disease. The evidence shows that decreasing the deer population actually increases Lyme disease, likely by increasing nymphal ticks feeding on mice. 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%).

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. 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, but they are not synchronized with the oaks. I live in the Pittsburgh area which is now a hotbed of Lyme Disease. During the 2017 season, I saw about 50 cases, once four cases in two hours, some of whom were quite sick. 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.

The first factor is the repopulation of areas with blacklegged ticks from reservoirs in the coastal northeast. Both of the 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 natives 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.

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.

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, and there are big health concerns from spraying insecticides in your yard. There are better ideas.

First, back in 1987, Thomas Mather at the University of Rhode Island Tick Encounter Resource Center developed a “drive-through” mouse trap (Damminix) 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 Home Depot or 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. This was never commercialized.

Changing suburban and rural landscaping to be less friendly to mice and ticks is recommended by the CDC (cdc.gov > Lyme Disease Home > Preventing tick bites). 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.

**Clinical Lyme Disease**

In the 19th century, syphilis was known as *The Great Imitator*, but in 21st century North America, that title has to 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 chronicum 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, the other two-thirds of the time it has central clearing; half of the time it will be on the lower extremities or buttocks. 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 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. The table provides the percentages of ***

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

**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 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 other picture 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 (it usually goes away in about 4 weeks), or by infection with *B. burgdorferi* without erythema migrans. The line 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 AV block. Treatment usually prevents these sequelae.

**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.

**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. But it’s quite unclear if all those with Bell’s Palsy in endemic areas need a workup for...
Lyme Disease, though there is a recommendation to obtain serological testing in endemic areas. Long-term follow-up of those with Lyme Bell's Palsy shows excellent results from standard treatment.

A percentage of untreated patients will have an indolent lymphocytic encephalitis-meningitis, 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, which can be treated by a month of IV ceftriaxone.

Cardiac involvement in Lyme Disease is most commonly heart block, but may also present as acute myocardiitis. 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.” 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. Those who get recurrent erythema migrans after antibiotic treatment is always reinfection, not recurrence of the original infection.

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 of 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.

If you have a patient in the ED with what looks like it might be erythema migrans, there is no point in sending any tests. Blood and skin biopsy cultures are only performed in research laboratories. Blood tests (serology) can be performed as a baseline, but 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, then 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.

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 Lyme Disease Antibodies, Including Reflex to Western Blot on Positives.

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: testing of individual ticks is not useful because:

- 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 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 this. 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.

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.

Pediatricians and pharmacologists are getting increasing nonchalant about prescribing doxycycline to kids and pregnant women. They certainly endorse doxycycline for Rocky Mountain Spotted Fever regardless of age, but there are still recommendations to avoid it for Lyme in kids less than 8 years old. Except that The Medical Letter says you can give kids under 8 a single prophylactic dose of doxycycline after a bite from an engorged Ixodes tick in an endemic area (see below).54,55

Cephalexin (e.g., Keflex)44 and penicillin and trimethoprim-sulfamethoxazole (e.g., Bactrim) and quinolones (e.g., Cipro, Levaxin) don’t work.55,56 Although erythromycin doesn’t work very well for Lyme, azithromycin (e.g., Zithromax) is a fourth-line choice, though instead of the standard “zpak” 5-day dose, some say you should prescribe 14 days.57,59

A better choice for older kids with penicillin allergy or those with contraindications for doxycycline is cefuroxime, which is safe even with a history of anaphylactic reactions to penicillin.60-62 and safe with pregnancy or breastfeeding. Cefuroxime is available as a relatively-inexpensive generic pill for children and as a brand-name liquid available as a relatively-inexpensive generic pill for adults and older kids, and as a brand-name liquid for younger kids. The pills are widely available, but as of 2017 only about a third of retail pharmacies as of 2017 only about a third of retail pharmacies reportedly stock them.57

A 2006 Clinical Guideline by the Infectious Diseases Society of America (IDSA) discusses prophylaxis and monitoring of those with tick bites:

A single dose of doxycycline may be offered to adult patients (200 mg dose) and to children >8 years of age (4 mg/kg up to a maximum dose of 200 mg) (BI) when all of the following circumstances exist: (a) the attached tick can be reliably identified as an adult or nymphal I. scapularis tick that is estimated to have been attached for >36 h on the basis of the degree of engorgement of the tick with blood or of certainty about the time of exposure to the tick; (b) prophylaxis can be started within 72 h of the time that the tick was removed; (c) ecologic information indicates that the local rate of infection of these ticks with B. burgdorferi is ≥20%; and (d) doxycycline treatment is not contraindicated. … Infection of ≥20% of ticks with B. burgdorferi generally occurs in parts of New England, in parts of the mid-Atlantic States [all of Pennsylvania now, and specifically 39% in western PA per a 2015 study56], and in parts of Minnesota and Wisconsin, but not in most other locations in the United States. … Doxycycline is relatively contraindicated in pregnant women and children <8 years old.

Persons who develop a skin lesion or viral infection–like illness within 1 month after removing an attached tick should promptly seek medical attention to assess the possibility of having acquired a tickborne infection.42

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., Ceftin) 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.46 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 referring. The follow-up physician could stop the antibiotics if another cause of the inflammatory arthritis becomes apparent.

The annual incidence of Lyme disease overall in endemic areas is about 100-200 per 100,000. About a third of reported cases are, or include,
arthritis. That means an incidence, again in endemic area, of 30-60/100,00. But the CDC suspect that only a tenth of cases are actually reported.44 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.42 Similarly, the incidence in one county in Minnesota is similarly about 50-60/100,000.43 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 (and kids, but see the section on RMSF below). The other problem I have with doxycycline is that I seem to see people with erythema migrans right before a summer vacation at the beach, and doxycycline is known to cause photodermatitis.

An important note: if you aren’t sure if what you see is cellulitis or erythema migrans, do not treat solely with cephalixin (e.g., Keflex) or trimethoprim-sulfamethoxazole (e.g., Bactrim); they are not effective against B. burgdorferi.44-46 So if you see “cellulitis” that’s not improving with one of these antibiotics, consider treating for erythema migrans.

More serious CNS disease (e.g., meningitis, encephalitis), or more serious arthritis or carditis, including those with a PR interval of greater than 0.3 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.43-45

One author recommends that any pregnant patient with any Lyme disease should be treated with 2 g of ceftriaxone IV daily for 14 days.71

LYME CONTROVERSY 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. 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.71

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.71

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.74

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:

- colloidal silver;
- intracellular hyperthermia therapy (ICH): 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, and
- infecting oneself with malaria.

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.75 One 30 year old woman died from an infected IV that had been in place for two years, for treatment of unsubstantiated Lyme disease.76 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”:77

- 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 woman in her 50s got weakness, swelling, and fever, and positive antibody tests, by themselves, do not result in persistent infection, variously called "chronic Lyme disease." And the chief of rheumatology at Tufts has been harassed, stalked, and threatened by reports in the popular press (see 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. 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. 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. In areas endemic for Lyme disease, the incidence of false-positive serologic results in patients with nonspecific myalgia or fatigue exceeds by four to one the incidence of true-positive results... And KLEMPNER showed, in placebo-controlled trials, that such patients do not benefit from ninety days of antibiotics.

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.
- Malarial 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.
- There is some evidence that B burgdorferi can hide and then erupt later, though others think this may be autoimmune phenomena 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 up to 10 years later have been positive. It is also likely that Lyme disease can trigger a variety of autoimmune sequelae, 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.

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, usually doxycycline, but for less than four weeks.

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.

**Other Tick-Associated Diseases**

**Anaplasmosis (Ehrlichiosis)**

The same *Ixodes* ticks that transmit *B. burgdorferi* may be infected with and transmit *Anaplasma phagocytophilum* (previously referred to as *Ehrlichia phagocytophila*), 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.

**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. 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.

*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.

At this rate, we will find a new doxycycline-responsive tickborne 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, parallel to 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 like a vaccine, making you create antibodies that protect you against *R. rickettsii* and RMSF.

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 ~20%. 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. The American Academy of Pediatrics says to use doxycycline for presumed RMSF or ehrlichial infection in children of any age.

**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
Tick paralysis is caused by a neurotoxin secreted in the saliva of certain ticks and is a well-known cause of illness 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.6 The saliva of Amblyomma americanum, the lone star tick, is known to induce anaphylactic allergy to a component of red meat (“alpha-gal”) in some who are bitten.7 So if you like steak, 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 used a thin red marker to draw a line on my skin, about 1/8” (3 mm), centered on the place where the pain had been. It was itchy. Unlike the rings of erythema migrans, this ring moved fast, maybe ½” (1 cm) per hour. And it kept spreading, and spreading. It spread over my entire body between two and three times. I could even see it moving across the sclera (white part) of my eyes. I had no other symptoms with it and it went away with no apparent lingering effects.


