Tick-borne Infections in California

Gary Green, MD, Anne Kjemtrup, PhD, DVM, and Michael Ferris

Disease	Tick vector to humans	Primary Reservoir(s)
Lyme disease	Western black-legged tick	Woodrat, white-footed mice, western tree squirrel
Tick-borne relapsing fever	Soft tick	Squirrels, chipmunks
Pacific Coast tick fever	Pacific Coast tick	Unknown
Rocky Mountain spotted fever	Pacific Coast tick, American dog tick, wood tick, brown dog tick	Rodents, dogs
Anaplasmosis	Western black-legged tick	Woodrat, white-footed mice
Tularemia	Pacific Coast tick, American dog tick	Rabbits, squirrels
Babesiosis	Unknown	Deer, bighorn sheep
Colorado tick fever	Wood tick	Unknown

Table 1. Tick-borne diseases endemic to California (listed in order of most to least commonly reported).

In the outdoors, our patients may experience bites from spiders, mosquitoes, ticks and deerflies. Each has a small risk of infection transmission, except for spiders, which have no transmission risk. This article addresses the vector part of the tick-borne disease equation in California, with an emphasis on northwestern coastal counties. Understanding more about the ecology of ticks can help physicians assess patient risks and also provide an opportunity for patient education.

Ticks are obligate blood-sucking arthropods. Worldwide and nationally, the list of tick-related pathogens continues to grow, with 13 currently identified in the United States. The pathogens are comprised of viruses (e.g., Powassan encephalitis virus), bacteria (e.g., *Borrelia burgdorferi*, the agent of Lyme disease), and protozoa (e.g., *Babesia microti*).[1] The geographic distribution and diversity of ticks and their respective pathogens is remarkably varied worldwide and within the United States, based on the complex interaction of the tick species (vector), the reservoir (mammals, birds, reptiles) and the habitat. In the northwestern coastal region, including Sonoma County, the number of possible tick-borne infections is few, and the risk of Lyme disease is much lower than in other parts of the nation.

Of the 47 species of ticks in California, eight consistently bite humans (see tables 1 and 2 for ticks of medical imporance).[2] There are two major tick families: *Argasidae* (soft ticks) and *Ixodidae* (hard ticks) that forage and feed quite differently. Three pertinent species of soft ticks in California inadvertently bite humans (*Ornithodoros hermsi, O. parkeri, O. coriaceus*). In California, *O. hermsi* is the most relevant soft tick for humans, as a bite from an infected tick can transmit the spirochete *Borrelia hermsii*, resulting in tick-borne relapsing fever (TBRF). In California, *O. hermsi* is mostly found between 1,000–2,700 meters of elevation.[3]

Most of the TBRF cases in California can be traced back to the Sierra and Transverse mountain ranges. Soft ticks reside in the nests or burrows of chipmunks and other small-mammal hosts, and they feed rapidly.[3] Staying in high-elevation cabins is the most common risk factor for TBRF because rodents build nests within the walls of cabins, bringing these ectoparasites with them. If rodents build nests in cabins and are then removed without concomitant ectoparasite control, people staying in

Dr. Green is chief of infectious diseases at Kaiser Permanente Santa Rosa. Dr. Kjemtrup is a research scientist at the California Dept. of Public Health. Mr. Ferris is the director of the Sonoma and Humboldt County public health laboratories.

those cabins are at risk of a bite from a soft tick in search of alternate hosts.

Most patients do not remember soft-tick bites because the ticks often bite at night and feed rapidly. In all three cases of TBRF diagnosed and treated at Santa Rosa Kaiser Medical Center since 2001, patients had recently traveled and stayed in the Sierras. None recalled a tick bite.

TBRF prevention is focused on avoiding tick bites. Keeping beds away from cabin walls, not sleeping on floors, and completely excluding rodents, including nest removal, are the mainstays of prevention.

The *Ixodidae* family (hard ticks) are nationally the most relevant family of ticks in clinical medicine. Hard ticks have a life-cycle consisting of egg, larva, nymph and adult (see figure 1).[2] After eggs hatch, each stage requires a blood meal to advance to the next stage, or the tick will perish.[2] Hard ticks feed on a variety of animals, including birds, mammals and, most important, reptiles. The larvae and nymphs feed on smaller animals (birds, small mammals, lizards) for about 2–4 days, while adults prefer medium- to large-size mammals (raccoons, coyotes, deer) and can feed for up to five days.[2]

Hard-tick nymphs and adults can bite humans. Nymphs are very small (poppy-seed size) and are hard to see with the naked eye; adults are larger (5–8 mm) and more easily seen. Because nymphs require moisture and humid environments, they are found in leaf litter under trees or on wood, such as fallen logs or picnic tables. In contrast, adults are found on grasses and low-lying shrubs.

Carbon dioxide exhaled from the host and/or host vibration are the principal stimuli for hard ticks to begin "questing" behavior (see figure 2).[4] They latch onto hosts that brush vegetation where they are foraging. They do not fly, jump or drop from trees, and they travel no more than a meter in search of a host.

Most hard-tick pathogens are not immediately transmitted when the tick begins to feed. Ticks often require 48 hours or more to scissor and grind through the epidermis of a host. They excrete digestive enzymes and anticoagulants to reach a blood vessel, where they transmit viral, bacterial or protozoa pathogens. *Borrelia burgdorferi*, the agent of Lyme disease, has other factors prolonging time for transmission. Before the spirochete can infect a host, it must alter outer-surface proteins in order to migrate from the gut to the salivary gland of the hard tick during feeding.[5] Removing a hard tick within 48 hours can usually prevent tick-borne pathogens from infecting the host. The exceptions are the Powassan virus on the East Coast,[6] and *Rickettsia rickettsii* (agent of Rocky Mountain spotted fever) from *Dermacentor* or *Rhipicephalus* ticks (in Southern California).[7]

California has three hard-tick species of medical importance: the Pacific Coast tick (*Dermacentor occidentalis*), the American dog tick (*D. variabilis*), and the western black-legged tick (*Ixodes pacificus*). The Pacific Coast tick is common throughout California, including the coastal region and the Sierras. The tick is the vector of the spotted-fever group of *Rickettsia*, which includes *Rickettsia rickettsii* (Rocky Mountain spotted fever), the recently described *Rickettsia phillipi* (Pacific Coast tick fever) and rarely the gram-negative coccobacilli, *Francisella tularensis* (tularemia). The American dog tick is found more diffusely throughout California and can also be a vector for Rocky Mountain spotted fever and tularemia (see table 2).

The western black-legged tick transmits *B. burgdorferi* (Lyme disease) and

Figure 1. Western black-legged tick life stages: (left to right) larvae, nymph, adult male, adult female.

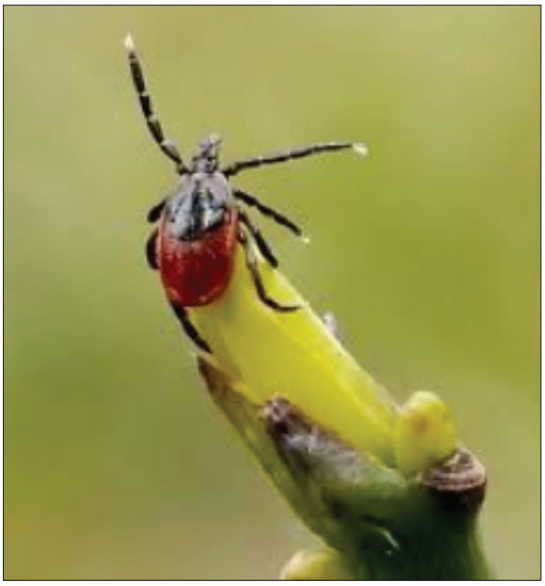

Figure 2. Western black-legged tick questing at the end of a grass awn, waiting for a host to brush against it.

Table 2. Human-biting ticks of California and diseases they transmit. (Photos courtesy CDPH.)

				
Western black-legged tick (female, male)	**American dog tick** (female, male)	**Pacific Coast tick** (female, male)	**Brown dog tick** (female)	**Soft tick**
Lyme disease	**Tularemia**	**Tularemia**	**Rocky Mountain spotted fever**	***B. hermsii*-associated TBRF**
Anaplasmosis	**Rocky Mountain spotted fever**	**Rocky Mountain spotted fever**		
		Pacific Coast tick fever		

the rickettsia-like pathogen *Anaplasma phagocytophilum* (human anaplasmosis).[8] The tick is found in moist coastal regions and the western side of the Sierras. The geography and ecology of Sonoma, Mendocino, Marin and Humboldt counties includes large areas of oak woodlands with moist coastal influences, an ideal environment for the western black-legged tick. It is the most common human-biting tick brought by patients to the Sonoma County Public Health Laboratory for tick identification and testing.[9]

New tick-borne pathogens continue to be studied in California. The malaria-like protozoa, *Babesia duncani,* is a rare tick pathogen in the western United States. The tick vector of *B. duncani* has not been discovered,[10] and clinical cases are confirmed in California only every 1–3 years.[11]

Borrelia miyamotoi is an emerging tick-borne spirochete pathogen in Europe and the East Coast, and it has been detected in almost 2% of the western black-legged ticks in California since 2000,[12,13] but no human cases have yet been confirmed in the state. Other interesting pathogens, such as a *Bartonella* species, are not yet identified as tick-borne. Many patients and some physicians prematurely consider *Bartonella* as a tick-borne pathogen. There is little evidence that *Bartonella* species can replicate within ticks, and no definitive evidence of transmission by a tick to a vertebrate host.[14]

The western black-legged tick has a three-year life cycle.[15] That life cycle helps explain the lower risk of acquiring Lyme disease in California, compared to the deer tick (*Ixodes scapularis*) of the East Coast and Midwest. Risk of Lyme disease infection is influenced by three factors: 1) the time of year tick life stages are active, 2) prevalence of *B. burgdorferi* in that tick stage and 3) length of time of tick attachment.

The seasonal Lyme disease risk period in California begins during the fall and winter months. Adult western black-legged female ticks start questing for a mammal host in October–November, often after a first rain.[16] If the adult female finds a blood meal and mates, she lays thousands of eggs—but there is no transovarial passage of *B. burgdorferi* or *A. phagocytophilum* to the eggs.[17,18]

In the spring, the eggs hatch into tick larvae and then molt into nymphs. Nymphal ticks feed actively and have a higher prevalence of *B. burgdorferi* than adult ticks. They also have a higher risk of infecting people because they are small and often not noticed, so they can feed longer without being disturbed.[16] Of the thousands of western black-legged ticks brought into the Sonoma County Public Health (SCPH) Laboratory during the winter and spring, only 23% are nymphal, demonstrating that adult stages are more often identified by patients.[9]

In California, the lower prevalence of *B. burgdorferi* in western black-legged ticks (compared to its prevalence in deer ticks in the East Coast and Midwest) and its higher prevalence in nymphal stages can be explained by the unique and important role of the western fence lizard (*Sceloporus occidentalis*) and the alligator lizard (*Elgaria multicarinata*). When an infected nymph takes a blood meal from its preferred lizard host, a protein of the alternate complement pathway of the lizard destroys the *B. burgdorferi* spirochete, "cleansing" it from the nymphal tick, with no harm to the lizard.[19]

This zooprophylaxis, discovered by Dr. Robert Lane at UC Berkeley, is a critical piece in understanding the lower prevalence of *B. burgdorferi* in nymphal and adult western black-legged ticks in California. The prevalence is typically 0–2% in adult ticks and 0–10% in nymphal ticks.[11] However, the risk of encountering an infected tick varies considerably, depending on local ecology, host availability, and many other factors.

A Mendocino County study demonstrated a 4.9% prevalence of *B. burgdorferi* in western black-legged nymphs, with the most infected nymphs detected in hardwood microhabitats (6.2%).[20] The prevalence was only 1.9% in redwood microhabitats and 0% in coastal pine habitats. A single sample tick prevalence of 22% was demonstrated but not consistently representative of any specific microhabitat region.

This environmental prevalence data stands in contrast to prevalence data

1. Information is based on Vector-Borne Disease Section, California Department of Public Health, tick collection records, 1910-2011. CDPH acknowledges local mosquito and vector control agencies who have contributed to these records.

2. Any information derived from this map is not an appropriate source for advice on tick exposure.

reported by the SCPH lab. Since 1996, nymph and adult western black-legged ticks brought by patients to the lab have been infected with *B. burgdorferi* at a prevalence consistently less than 2%.[9] In other words, more than 98% of those ticks have no detectable *B. burgdorferi*.

Time of tick attachment is also important for transmission of *B. burgdorferi*. In one study, researchers allowed a highly virulent strain of *B. burgdorferi* to infect western black-legged nymphs and feed on deer mice for varying lengths of time.[21] At 24, 48 and 72 hours of tick feeding, 0%, 11%, and 25% of the mice became infected with *B. burgdorferi*, respectively. When nymphs were left to feed for more than 96 hours, over 80% of the mice became infected with *B. burgdorferi*. It takes at least 48 hours for nymphal western black-legged ticks to transmit the *B. burgdorferi* pathogen, so patients and physicians have ample opportunity to remove an infected tick without the patient becoming infected. Determining how long a tick has been feeding can be difficult, but a fully engorged tick has been attached for a longer period of time.

Because of the lower spirochete prevalence in local western black-legged ticks, the wide microhabitat variability of *B. burgdorferi* prevalence, and the longer time required for tick attachment to transmit the pathogen, the risk of Lyme disease is much lower in California than in other parts of the country. In one epidemiological model of *B. burgdorferi* transmission in California, researchers quantified the risk of western black-legged ticks carrying Lyme disease as follows: A western black-legged tick attached for an undetermined period of time has an average risk for

spirochete transmission of 0.0005% to 0.004%.[22] In other words, the risk of getting Lyme disease in California from the bite of a western black-legged tick is between five chances in 10,000 to four chances in 1,000.

Coinfection with *B. burgdorferi* and *A. phagocytophilum* is rare in the western black-legged tick, in contrast to the deer tick of the East Coast and Midwest, where 4–28% can be infected with *B. burgdorferi, E. chaffeensis, A. phagocytophilum* and/or *B. microti*.[23] In a Mendocino County study, 3.4% of 234 nymph western black-legged ticks were infected with *A. phagocytophilum*, and 3.9% of 234 nymph ticks were infected with *B. burgdorferi,* but only two ticks had both pathogens.[24] A later Mendocino study found a nymph coinfection rate of only 0.27% in western black-legged ticks.[25] Coinfection with *B. burgdorferi* and *A. phagocytophilum* in western black-legged ticks is rare, and it never includes *B. duncani.*

Many California patients feel anxious about deer ticks, even though this species is only found in the East Coast and Midwest. However, since patients travel, Lyme disease is reported in California in patients who visit these areas.

Deer ticks have a two-year life cycle, with nymphs feeding on white-footed mice, and adults feeding on white-tailed deer. No lizards are involved at either stage. Nymph deer ticks (the principal Lyme disease vector) are most active in spring and summer, so Lyme disease in the East Coast and Midwest is a "summertime" disease, while Lyme disease in California peaks about a month earlier, in late spring.[16] Coinfection is much more common in deer ticks than in western black-legged ticks.

California patients frequently express a fear of Lyme disease in relation to the density of deer in their neighborhood. In fact, deer do not transmit the spirochete to deer ticks, although they can increase the number of deer ticks in the environment.

Patients often feel anxious when they discover an attached tick. They should be advised to remove the tick appropriately as soon as it is discovered, using a pair of fine-tipped forceps or available tweezers. The attached tick should be grasped at the mouthparts as close to the insertion point as possible and pulled firmly and gently straight out (see figure 3). The tick should not be twisted or turned, as the mouthparts may separate from the tick's body and remain embedded in the skin. Applying a lighted match, gasoline or "bug spray" are ineffective and potentially dangerous procedures.

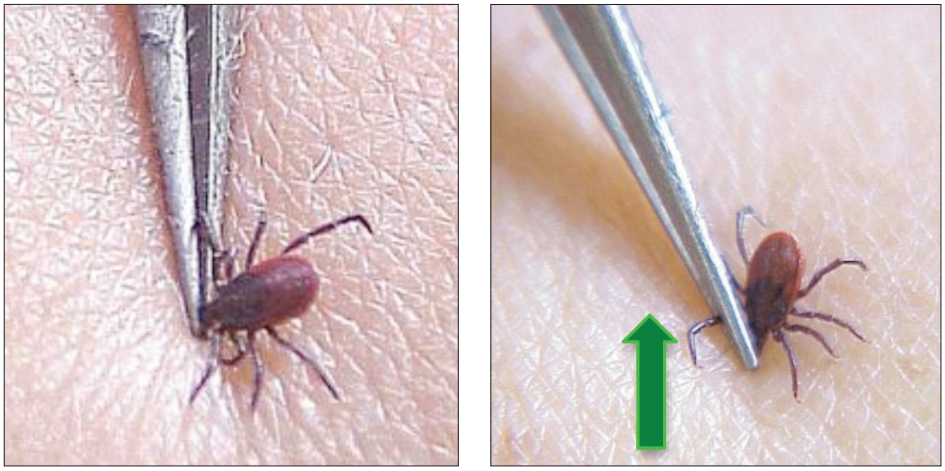

Figure 3. Tick removal: (1) Use forceps to grasp the tick at the mouthparts as close to the insertion point as possible. (2) Firmly and gently pull the tick up and out.

Patients should clean the area of the bite with soap and water, and keep it dry. If tick mouthparts are retained in the skin, they may produce a pruritic tick granuloma that may eventually extrude from the epidermis, similar to a wood sliver. A physician can remove the granulomatous embedded mouthparts with a small punch biopsy. Retained tick mouthparts in the skin do not present a disease risk.

Repeated bites from western black-legged ticks, with their unique salivary proteins and reversed mouthpart barbs, can produce a small (<3 cm), red, pruritic or painful lesion within hours or a few days after the tick bite. This allergic and sometimes inflammatory reaction should not be confused with erythema migrans, the diagnostic rash of Lyme disease, which is usually not painful, appears three days or more after a bite from an infected tick, and expands. The tick can be retained for species identification, but testing for

Table 3. Tick Avoidance Guidance from the CDC

Avoid direct contact with ticks

- Avoid wooded and bushy areas with high grass and leaf litter.
- Walk in the center of trails.

Repel ticks with DEET or permethrin

- Use repellents with 20-30% DEET on exposed skin and clothing. Protection lasts up to several hours. Always follow product instructions. Parents should apply this product to their children, avoiding hands, eyes and mouth.
- Treat clothing and gear, such as boots, pants, socks and tents with products containing 0.5% permethrin, which remains protective through several washings. Pretreated clothing is available and may be protective longer.

Find and remove ticks from your body

- Bathe/shower after coming indoors (preferably within two hours) to wash off and more easily find ticks that are crawling on you.
- Conduct a full-body tick check using a hand-held or full-length mirror. Parents should check their children for ticks under the arms, in and around the ears, inside the belly button, behind the knees, between the legs, around the waist, and especially in their hair.
- Examine gear and pets. Ticks can ride into the home on clothing and pets.
- Tumble clothes in a dryer on high heat for an hour to kill remaining ticks.

the presence of *B. burgdorferi* should not be done solely for individual medical decision making.[26]

In summary, the unique ecology of California contributes to a tick fauna and accompanying disease epidemiology different from that of other areas of the United States. The ecology of western black-legged ticks results in less prevalence of disease agents and a tick seasonality more associated with spring and fall than with summer. This knowledge allows physicians to assess patient risk for Lyme disease and other tick-borne infections. We can help our patients avoid tick bites by following a few simple CDC recommendations (see table 3).[27]

For more information on tick-borne diseases in California, visit www.cdph.ca.gov. A CDPH map showing the distribution of western black-legged ticks can be found on page 8 of this article. ◇

Email: garygreenmd@gmail.com

References

1. Brett ME, et al, "U.S. healthcare providers' experience with Lyme and other tick-borne diseases," *Ticks & Tick-Borne Dis,* 5:404-408 (2014).
2. Furman DP, Loomis EC, "Ticks of California," *Bulletin of the California Insect Survey,* 25 (July 1984).
3. Fritz CL, et al, "Serologic evidence for *B. hermsii* infection in rodents on federally owned recreational areas in California," *Vector-Borne & Zoonotic Dis,* 13:376-381 (2013).
4. Garcia R, "Collection of *D. andersoni* with carbon dioxide and its application in studies of Colorado tick fever virus," *Am J Trop Med Hyg,* 14:1090-93 (1965).
5. Joppe WR, et al, "Tick-host-pathogen interactions in the post-genomic era," *Trends Parisitol,* 23:434–438 (2007).
6. Dupuis A, et al, "Isolation of deer tick virus from *I. scapularis* and detection of antibody in vertebrate hosts sampled in the Hudson Valley," *Parasites Vect,* DOI: 10.1186/1756-3305-6-185 (2013).
7. Warner RD, Marsh WW, "Rocky Mountain spotted fever," *J Am Vet Med Assoc,* 221:10 (2002).
8. Dumler JS, Walker DH, "Tick-borne ehrlichiosis," *Lancet Infec Dis* (April 2001).
9. Ferris M, internal laboratory testing data, Sonoma County Public Health Laboratory.
10. Kjemtrup A, "Molecular epidemiology of human babesiosis in California," Shields Special Collections LD781.D5j (2001).
11. CDPH-VBDS, Annual Report, www.cdph.ca.gov (2001).
12. Padgett K, et al, "Large scale spatial risk and comparative prevalence of *B. miyamotoi & B. burgdorferi sensu lato in I. pacificus,*" accepted for publication, PLOS ONE (2014).
13. Munab J, et al, "Detection of a *B. miyamotoi sensu lato* relapsing-fever group spirochete from *I. pacificus* in California," *J Med Ento,* 43:120-123 (2006).
14. Angelakis E, et al, "Potential for tick-borne Bartonelloses," *Emerging Infec Dis,* 16:385-391 (2010).
15. Padget KA, Lane RS, "Life cycle of *I. pacificus*," *J Med Ento,* 38:684-693 (2001).
16. Salkelda DJ, et al, "Seasonal activity patterns of the western black-legged tick," *Ticks & Tick-borne Dis,* in press (2014).
17. Rollend L, et al, "Transovarial transmission of Borrelia spirochetes by *I. scapularis*," *Ticks & Tick-Borne Dis,* 4:46–51 (2013).
18. Rikihisa Y, "Mechanisms of obligatory intracellular infection with *A. phagocytophilum*," *Clin Microbiol Rev,* 24:469-489 (2011).
19. Kuo MM, et al, "Comparative study of mammalian and reptilian alternative pathway of complement-mediated killing of the Lyme disease spirochete," *J Parasitol,* 86:1223-28 (2000).
20. Eisen RJ, et al, "Spatially explicit model of acarological risk of exposure to *B. burgdorferi*-infected *I. pacificus* nymphs in northwestern California based on woodland type, temperature, and water vapor," *Ticks & Tick-Borne Dis,* 1:35-43 (2010).
21. Peavey CA, Lane RS, "Transmission of *B. burgdorferi* by *I. pacificus* nymphs and reservoir competence of deer mice infected by tick bite," *J Parasitol,* 81:175–178 (1995).
22. Fritz CL, Vugia DJ, "Clinical issues in Lyme borreliosis," *Infec Dis Rev,* 3:111-122 (2001).
23. Swanson SJ, et al, "Coinfections acquired from *Ixodes* ticks," *Clin Microbiol Rev,* 19:708–727 (2006).
24. Lane RS, et al, "Human behaviors elevating exposure to *I. pacificus* nymphs and their associated bacterial zoonotic agents in a hardwood forest," *J Med Entomol,* 41:239-248 (2004).
25. Lane RS, et al, "Host-seeking behavior of *I. pacificus* nymphs in relation to environmental parameters in dense-woodland and woodland-grass habitats," *J Vector Ecol,* 32:342-357 (2007).
26. Wormser GP, et al, "Clinical assessment, treatment and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis," *Clin Infect Dis,* 43:1089-34 (2006).
27. CDC, "Preventing tick bites, www.cdc.gov (2011).