



County of Napa
Health and Human Services Agency
Public Health Division



Physician Advisory Lyme Disease and Other Tick-Borne Diseases

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To: Napa County Physicians

From: Karen Smith, MD, MPH
Public Health Officer

As the temperature warms up and Californians start spending more time outdoors their risk of a tick bite increases. "Nymphs," or immature form of the western black-legged ticks, which transmit Lyme Disease (LD), are most active during the spring and early summer months. This advisory is to review the salient clinical characteristics of LD, to provide guidelines on diagnosis and treatment, to provide instruction for reporting cases, to briefly cover other tick-borne illnesses and to provide guidance on when to submit ticks for testing.

According to the 2006 Vector Borne Diseases in California 2006 Annual Report from the California Department of Public Health (CDPH0, the incidence of LD in Napa was 1.2 cases/100,000 person years from 1997 – 2006.

LYME DISEASE

Background

Lyme Disease (LD) was first described in 1977 as a cluster of oligoarticular arthritis in children and adults near Lyme, Connecticut. The spirochetal agent of LD is *Borrelia burgdorferi*, which is transmitted by the bite of an infected tick vector. The CDC made LD a nationally notifiable condition in 1982. Title 17 of the California Code of Regulations requires that physicians report all newly diagnosed cases of LD to their local health departments. The first recognized human case in California occurred in 1978 in a hiker from Sonoma County. As of 2000, the CDPH has reported 1,700 of LD from 52 of 58 counties.

Transmission

In California, the bacterium (*B. burgdorferi*) that causes LD is transmitted to humans by the western black-legged tick, *Ixodes pacificus*, which has three life stages: larva, nymph, and adult. Only nymphs and adult ticks can transmit the infection to humans. Nymphs are most active from March through July, while adults are most active November through March. However, if conditions are favorable, ticks can be active year-round.

The CDPH Vector Borne Diseases section regularly conducts surveillance for *Ixodes pacificus* in Bothe-Napa Valley State Park where pooled samples of ticks first tested positive for *Borrelia burgdorferi* in 2005.

Factors Affecting Transmission of Lyme Disease

Tick type – *B. burgdorferi* is only transmitted by ticks of the genus *Ixodes*, and most infections are transmitted by nymphal ticks which are approximately the size of poppy seeds (as opposed to the dog tick which is about the size of a pencil eraser).

Tick attachment – *B. bergdorferi* is rarely transmitted within the first 48 hours of tick attachment. By that time the tick is fully engorged and globular in shape. The risk of transmission is, therefore, much higher if the identified tick is at least partially engorged.

Clinical Illness

LD can be difficult to diagnose, starting as a mild flu-like illness and, over time, developing into severe chronic health problems affecting multiple body systems.

Early Symptoms

Early symptoms of LD present 3 to 30 days after the bite from an infected tick. Erythema migrans (EM) is described as a red, blotchy expanding rash, accompanied by fever, headache, neckache, muscle and joint pain. The EM is present in 70-80% of infected persons, but may go undetected by a patient or physician if it occurs in a location difficult to see (e.g., scalp) or if the patient has dark skin. One or more EM rashes can occur, not necessarily at the site of the tick bite. The rash can precede, accompany, or follow flu-like symptoms.

Occasionally, an allergic reaction to the saliva of the tick can occur on the skin and may be mistaken for EM. Unlike EM, the allergic reaction occurs within minutes to hours of the tick bite and does not spread.

Later Symptoms

Weeks to months after the bite of an infected tick, the spirochetes disseminate, resulting in cardiac conduction defects (atrio-ventricular block) and cranial and peripheral neuropathies often exhibited as a unilateral facial palsy, or numbness and pain in arms and legs. If left untreated or improperly treated, late LD can occur weeks, months or years after infection. Chronic arthritis, manifested as recurrent swelling of one or a few joints, is the most common feature. Chronic muscle pain and encephalopathies, such as memory loss and difficulty concentrating may also be present.

Diagnosis

Clinical Suspicion and Tick Testing

Diagnosis of LD is based primarily on clinical presentation and supportive history, specifically risk of exposure to infected ticks, and confirmed by specific laboratory tests. The CDPH does not recommend ticks that have been attached to a person be tested to determine if medical treatment is necessary because 1) testing methods vary in accuracy, 2) the need for treatment should not be based on these results, and 3) tick testing results do not necessarily predict if the person bitten will develop LD. Even if an attached tick tests negative, other undetected ticks may have attached to a person and transmitted *B. burgdorferi*.

Laboratory Diagnosis

A two-test approach for active disease and for previous infection using a sensitive enzyme immunoassay (ELISA) or immunofluorescent assay (IFA) followed by a Western immunoblot is the algorithm of choice. All specimens positive or equivocal by a sensitive ELISA or IFA should be tested by a standardized Western immunoblot. Specimens negative by a sensitive ELISA or IFA need not be tested further.

When Western immunoblot is used within the first 4 weeks of disease onset, both immunoglobulin M (IgM) and immunoglobulin G (IgG) procedures should be performed. A positive IgM test result alone is not recommended for use in determining active disease in person with illness greater than 1 month's duration because the likelihood of a false-positive test result for a current infection is high for these persons. Western immunoblot IgM diagnostic bands include 24, 39, and 41 kDa. Western immunoblot IgG diagnostic bands include 18, 21, 28, 30, 39, 41, 45, 58, 66, and 93 kDa. If a patient with suspected early LD has a negative serology, serologic evidence of infection is best obtained by testing of paired acute- and convalescent-phase serum samples. Serum samples from persons with disseminated or late-stage LD almost always have a strong IgG response to *B. burgdorferi* antigens.

The value of acute and convalescent sera to diagnose Lyme Disease in asymptomatic persons who report tick bite is not proven even in areas with high rates of tick infection. For this reason, serologic testing following a tick bite is NOT recommended.

In 2005, the CDC and FDA became aware of commercial laboratories that conduct LD testing by using assays whose accuracy and clinical usefulness have not been established. These tests include urine antigen tests, immunofluorescent staining for cell wall—deficient forms of *B. burgdorferi*, and lymphocyte transformation tests. Additionally, some laboratories perform polymerase chain reaction tests for *B. burgdorferi* DNA on inappropriate specimens such as blood and urine or interpret Western blot using criteria that have not been validated and published in peer-reviewed scientific literature.

Prophylaxis

Proper tick removal is important in people who discover an attached tick on their body (see below). The Infectious Diseases Society of America recommends that antibiotic prophylaxis be given ONLY in patients who meet all of the following criteria:

- Attached tick is an adult or nymphal *Ixodes* tick.
- Tick is estimated to have been attached for at least 36 hours (estimated by engorgement or recalled time of exposure).
- Prophylaxis is begun within 72 hours of tick removal.
- Rate of infection in the geographic area where tick bite occurred is at least 20%. (NOTE: this rate is seen only in parts of New England, the mid-Atlantic states, and parts of Minnesota and Wisconsin. In 2006 only 2.0% of ticks tested in California were positive.)
- The patient has no contraindication to doxycycline.

For patients who meet the criteria for prophylaxis the recommended dose of doxycycline is a single dose of 200 mg for adults and 4 mg/kg to a maximum of 200 mg for children over 8 years. Wormser GP *et al.* The Clinical Assessment, Treatment, and Prevention of Lyme Disease, Human Granulocytic Anaplasmosis, and Babesiosis: Clinical Practice Guidelines by the Infectious Diseases Society of America, *Clinical Infectious Diseases* 2006;43:1089–1134.

<http://www.journals.uchicago.edu/doi/full/10.1086/508667>.

Treatment

In adult patients, the recommended treatment for early localized or early disseminated Lyme disease associated with EM, in the absence of specific neurological manifestations or advanced atrioventricular heart block, is doxycycline (100 mg twice per day), amoxicillin (500 mg 3 times per day), or cefuroxime axetil (500 mg twice per day) for 14 days (range, 10–21 days for doxycycline and 14–21 days for amoxicillin or cefuroxime axetil). Antibiotics recommended for children are amoxicillin (50 mg/kg per day in 3 divided doses [maximum of 500 mg per dose]), cefuroxime axetil (30 mg/kg per day in 2 divided doses [maximum of 500 mg per dose]), or, if the patient is ≥ 8 years of age, doxycycline (4 mg/kg per day in 2 divided doses [maximum of 100 mg per dose]).

Patients treated with antibiotics in the early stages of the infection usually recover rapidly and completely. A few patients, particularly those diagnosed with later stages of disease, may have persistent or recurrent symptoms. These patients may benefit from a second 4-week course of therapy. Longer courses of antibiotic treatment have not been shown to be beneficial and have been linked to serious complications, including death. Patients with certain neurological or cardiac forms of illness may require intravenous treatment with drugs such as ceftriaxone or penicillin. For guidelines on treatment of the later stages of LD, please see: Wormser GP *et al.* (reference above).

OTHER TICK-BORNE DISEASES

Human Granulocytic Anaplasmosis (HGA)

Most cases of HGA (formerly known as human granulocytic ehrlichiosis) occur in the upper Midwest and northeastern United States. It is an uncommon infection in California, which only had 6 confirmed cases between 1994 and 2006.

Transmission

Human infection with *Anaplasma phagocytophilum*, the agent of HGA, occurs in areas of the United States and Europe where Lyme disease is endemic. *A. phagocytophilum* is transmitted through the bite of infected *Ixodes* ticks.

Clinical Illness

Most individuals have no or mild symptoms. Symptoms usually present as an influenza-like illness within two to three weeks after the bite. Some patients may develop a rash.

Diagnosis and Treatment

Indirect fluorescent antibody (IFA) assay of acute-phase *and* convalescent-phase sera is the most sensitive diagnostic method. Identification of the characteristic intragranulocytic inclusions on blood smear is a rapid diagnostic method, but is considered less sensitive as such inclusions are often scant in number or sometimes absent. Doxycycline and rifampin are both active against *A. phagocytophilum*.

Babesiosis

Babesiosis is caused by hemoprotozoan parasites of the genus *Babesia*. Most cases of babesiosis in the US are caused by *Babesia microti*, found in deer ticks (*Ixodes scapularis*) which occur in the Northeast and Midwest. Additionally, *Babesia duncani* has been identified in cases of babesiosis in California and Washington.

Transmission

Transmission of *B. microti* is through the bite of an infected deer tick. The vector for *B. duncani* is currently unknown.

Clinical Illness

Most individuals have no or mild symptoms. Manifestations of disease include fever, chills, sweating, myalgias, fatigue, hepatosplenomegaly, and hemolytic anemia. Symptoms typically occur after an incubation period of 1 to 4 weeks, and can last several weeks. The disease is more severe in patients who are immunosuppressed, splenectomized, and/or elderly.

Diagnosis and Treatment

Diagnosis of *Babesia* infection should be made by detection of parasites in patients' blood smears. However, antibody detection tests are useful for detecting infected individuals with very low levels of parasitemia (such as asymptomatic blood donors in transfusion-associated cases), for diagnosis after infection is cleared by therapy, and for discrimination between *Plasmodium falciparum* and *Babesia* infection in patients whose blood smear examinations are inconclusive and whose travel histories cannot exclude either parasite. Drugs used to treat babesiosis are similar to those used to treat malaria. Treatment with clindamycin plus quinine or atovaquone plus azithromycin are also options. Severe cases may require a blood transfusion.

Tick-borne Relapsing Fever (TBRF)

TBRF is an infection caused by *Borrelia hermsii*. Most infections in California occur in people who have vacationed in rural mountain areas (3000 and 9000 feet) between May and September.

Transmission

Transmission is through the bite of a soft tick infected with *Borrelia hermsii*, which often occurs while sleeping in a rodent infested building. Soft ticks live in cool, dark places, such as shaded wood piles outside buildings and between walls or beneath floorboards. Most people do not realize they were bitten because soft ticks feed mostly at night and remain attached for only a few minutes.

Clinical Illness

TBRF is a disease characterized by relapsing (*i.e.* recurring) episodes of fever, often accompanied by other symptoms. The incubation period ranges from 2 to 18 days. Initial symptoms include sudden fever (104-105°F), chills, headache, arthralgia and myalgia. Nausea, vomiting, abdominal pain and rash may also occur. Symptoms are typically present for 3 to 5 days before abruptly disappearing. Length of time before reoccurrence of symptoms ranges from 4 to 14 days; relapses may occur up to 10 times in untreated persons.

Diagnosis and Treatment

The definitive diagnosis of TBRF is based on the observation of *Borrelia* spirochetes in smears of peripheral blood, bone marrow, or cerebrospinal fluid in a symptomatic person. Although not valuable for making an immediate diagnosis, serologic testing is available through public health laboratories and some private laboratories. Acute serum should be taken within 7 days of symptom onset and convalescent serum should be taken at least 21 days after symptoms start. Spirochetes are most commonly seen in blood samples obtained during a period of fever. Erythromycin, tetracyclines, chloramphenicol, or penicillins have all been shown to be effective for treating TBRF. Although duration of therapy has not been well studied for TBRF, the current recommendation is 7 days of antibiotic therapy.

Rocky Mountain Spotted Fever (RMSF)

RMSF is a serious and potentially life threatening infection caused by *Rickettsia rickettsii*. Cases occur most frequently between April and September, with a few cases reported in California every year.

Transmission

Rickettsia rickettsii is transmitted through the bite of an infected tick, most commonly the Pacific Coast tick, *Dermacentor occidentalis*, in California. The Rocky Mountain wood tick, *Dermacentor andersoni*, may also transmit the infection in California.

Clinical Illness

RMSF is characterized by sudden onset of symptoms 2 to 14 days after a tick bite; initial symptoms may include fever, nausea, vomiting, severe headache, muscle pain, and lack of appetite. Severe cases can result in kidney failure and death. The characteristic red, spotted (petechial) rash of RMSF is usually not seen until the sixth day or later after onset of symptoms, and this type of rash occurs in only 35% to 60% of patients with RMSF. The rash involves the palms or soles in as many as 50% to 80% of patients. Up to 25% of patients who receive delayed or no treatment may die.

Diagnosis and Treatment

Early diagnosis for RMSF relies on symptoms and history or suspicion of a tick bite. Routine clinical laboratory findings suggestive of RMSF may include abnormal white blood cell count, thrombocytopenia, hyponatremia, or elevated liver enzyme level. Serologic assays, such as IFA testing of acute and convalescent serum, may be used for confirmation of RMSF cases. ***Treatment decisions should be based on epidemiologic and clinical clues, and should never be delayed while waiting for confirmation by laboratory results.*** Doxycycline (100 mg every 12 hours for adults or 4 mg/kg body weight per day in two divided doses for children under 45 kg [100 lbs]) is the drug of choice for patients with RMSF and should generally be given for a minimum of 5 to 10 days.

Tick Paralysis

Tick paralysis is caused by a reaction to a chemical in the tick's saliva, resulting in inhibition of the normal functions of nerves and muscles.

Transmission

A tick must be attached to the skin for tick paralysis to occur. In the Pacific Northwest and Rocky Mountain states, most cases of tick paralysis are caused by the Rocky Mountain wood tick.

Clinical Illness

Two to seven days after a tick bite the patient feels weakness in the arms and legs. Hours to days later, patients become unable to move their arms and legs. If not treated, patients may become unable to speak or breathe. Tick paralysis may resemble botulism and other nervous system disorders.

Diagnosis and Treatment

Locating and removing the attached tick(s) is the only necessary treatment. In most cases, normal muscle function returns within hours of removing the tick(s).

Tularemia

Tularemia is a potentially serious infection caused by *Francisella tularensis*. Several animals can serve as reservoirs for *Francisella tularensis*, with the most common being rodents, rabbits and hares.

Transmission

People can get tularemia in many different ways, including being bitten by an infected tick or deerfly, handling infected animal carcasses, eating or drinking contaminated food or water, and through inhalation of aerosolized bacteria (e.g. after hitting an infected rabbit with a lawn mower or as a result of bioterrorism). Hunters, trappers, wildlife specialists, and others who handle or eat infected animals are at higher risk of infection. Tularemia is not known to be spread from person to person.

Clinical Illness

Symptoms in humans appear about 3 to 6 days after infection and often present as an influenza-like illness with fever, headache, diarrhea, joint pain, myalgia, etc. Chest pain and bloody sputum may occur as a result of pneumonia. Depending on the route of exposure, infected persons may develop ulcers on the skin or mouth, swollen and painful lymph glands, swollen and painful eyes, or a sore throat.

Diagnosis and Treatment

Serology is most commonly used for diagnosis. Streptomycin (7.5 mg/kg IM q 12 hours x 10-14 days) or Gentamycin (3-5 mg/kg/day IV or IM qd in 3 divided doses x 10-14 days) are the preferred antibiotics. Tetracyclines given for at least 14 days are alternative choices, although they are bacteriostatic and associated with higher relapse rates.

PREVENTION OF TICK-BORNE DISEASE

Tick avoidance remains the best line of defense against LD and other tick-borne diseases. Avoiding areas where ticks are known to occur will largely prevent tick-borne diseases. Ticks prefer cool, moist environments and can be found on wild grasses and low vegetation in both urban and rural areas. Adult ticks climb to the tip of vegetation along animal trails and wait for a host to brush against them. Nymphs are found in low, moist vegetation such as leaf litter. For prevention of Lyme disease after a recognized tick bite, routine use of antimicrobial prophylaxis or serologic testing is generally not recommended because it is of unproven value and is associated with potential risks and costs.

People who live or recreate in areas where ticks occur should be advised to:

- Wear long pants and long-sleeved shirts; tuck pant legs into boots or socks; tuck shirts into pants.
- Wear light-colored clothing so ticks can easily be seen.

- Apply insect repellent registered for use against ticks to clothing, following directions on the container and taking extra care when applying repellent to children.
- Stay in the middle of the trail; avoid trail margins, brush and grassy areas.
- Keep grass along trails, buildings and camping areas mown.
- Inspect yourself frequently for ticks when in tick habitat.
- Once out of tick habitat, thoroughly check your entire body for ticks; parents should examine their children, especially on the scalp and hairline.
- Remove ticks promptly to decrease the risk of spirochete or other infective agent transmission.

If a person finds a tick on their body, they should be advised to:

- Use tweezers to grasp the tick's mouthparts as close to the skin as possible.
- Gently pull the tick straight out, using a firm steady motion.
- DO NOT jerk, twist or burn the tick.
- Wash hands and bite site with soap and water; apply antiseptic to the bite site.
- Consult a physician if you develop any symptoms, especially a rash, within 30 days of the tick bite.

REPORTING OF TICK-BORNE DISEASES

Lyme disease, human granulocytic anaplasmosis, babesiosis, tick borne relapsing fever, Rocky Mountain Spotted Fever, and tularemia are all reportable to the Napa County Public Health Division. Tularemia should be reported immediately, including after hours. Babesiosis and relapsing fever should be reported within one working day; Lyme disease, human granulocytic anaplasmosis, and Rocky Mountain Spotted Fever within seven calendar days. Confidential Morbidity Report (CMR) forms can be found on the Public Health Website at www.co.napa.ca.us/publichealth under Communicable Disease Report. Reports can be faxed or called in to:

Napa County Public Health Division
 Tel: (707) 299 -1499
 Fax: (707) 299-4479
 Tel after hours: (707) 265-3131 (for diseases requiring immediate notification only)

Sincerely,



Karen L. Smith, MD, MPH
 Public Health Officer