Tick-borne diseases are the most common vector-borne illnesses in the United States. Lyme disease is the most common, but several others also occur. The ehrlichioses have only been identified as agents of human disease in the United States in the past few decades, and knowledge about them is still evolving. Rocky Mountain spotted fever is relatively common and can be severe, especially in children, if the diagnosis is not made quickly. Tularemia has long been known to cause disease in humans, but there is renewed interest because of its potential as a biologic warfare agent. These diseases can be severe or even fatal. Most of them are easily treatable when identified early. These diseases result from a variety of infectious agents including bacteria, rickettsia, viruses and protozoa, or they may be caused by substances produced by the tick. Most of these diseases present initially with nonspecific symptoms and are often difficult to recognize. Few definitive diagnostic tests are available. Therefore, knowledge of the epidemiology and common presentations, as well as the diagnostic options and treatments available, are important issues for family physicians. (Am Fam Physician 2001; 64:461-6, 468.)

Ticks are members of the class Arachnida. There are three families of ticks, two of which are known to transmit disease to humans. The family Ixodidae includes 13 genera, of which Amblyomma, Dermacentor and Ixodes transmit disease to humans in the United States. The family Argasidae contains five genera; only Ornithodoros is known to transmit disease to humans in the United States. The mechanism of transmission of disease through tick bites is not well understood. During a blood meal, pathogens harbored in the gut of ticks may migrate to their salivary glands and then are transmitted to the host. When a tick attaches to a human, prostaglandins in the tick saliva are passed into the skin. These prostaglandins may decrease the production of IL-1 and TNF-alpha by macrophages and the secretion of IL-2 and interferon gamma by T-lymphocytes. These actions have an inhibitory action on the host’s local immune response. Apyrase, an enzyme in tick saliva, may maintain blood flow into the bite by stimulating local vasodilation and preventing platelet aggregation. There are also inhibitors of the coagulation cascade in tick saliva that enhance blood flow to the lesion. These factors combine to enhance the blood meal of the tick and facilitate transmission of infectious agents to the host. Table 1 summarizes the most common tick-borne diseases.

Lyme Disease

Lyme disease, caused by the spirochete Borrelia burgdorferi, is the most common vector-borne illness in the United States. The disease was first characterized in the mid-1970s, but B. burgdorferi was not isolated as the causative agent until the early 1980s. In 1999, 16,273 cases of Lyme disease were reported to the Centers for Disease Control and Prevention (CDC). The disease has a bimodal age distribution with peaks in patients younger than 15 and older than 29 years. Most cases occur from May through September. Although it has been reported in 48 states, approximately 90 percent of cases occur in the Northeast, upper Midwest and northern California.
Lyme disease has three stages. The early localized stage begins days to weeks following the tick bite and is characterized by erythema chronicum migrans. This lesion occurs in 60 to 80 percent of cases. It begins as a small red papule at the site of the bite, expanding centrifugally over days to weeks. A central punctum often remains hyperemic, raised or scaly. The lesion may reach 28 in (70 cm) in diameter; the average is about 6.4 in (16 cm). The central clearing of the lesion, once emphasized, is now thought to occur in about one third of cases. Mild systemic symptoms may accompany the rash including fatigue, myalgias, arthralgias, headache, fever and chills. Physical examination may reveal neck stiffness, regional adenopathy and secondary skin lesions smaller than the primary lesion and not associated with the site of the tick bite. Untreated, the lesions usually resolve over several weeks.

The early disseminated form of Lyme disease occurs days to months after the tick bite and may present with symptoms involving many systems. Many patients will not recall a tick bite. Patients may or may not have had erythema chronicum migrans. Patients may present with neurologic symptoms including lymphocytic meningitis, cranial nerve palsies (most commonly Bell's palsy), and painful radiculoneuritis followed by decreased sensation, weakness and absent reflexes. Cardiac symptoms occur most commonly in men and present as weakness, fatigue and palpitations. There may be varying degrees of atrioventricular block and a mild pericarditis or myocarditis. Arthritis is usually a late manifestation but also may occur at this stage.

### TABLE 1

<table>
<thead>
<tr>
<th>Tick-borne Diseases</th>
<th>Geographic distribution</th>
<th>Common presenting symptoms</th>
<th>Initial laboratory findings</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lyme disease</strong></td>
<td>Northeast and upper Midwest</td>
<td>Erythema migrans, fatigue, myalgias, arthralgias, headache, fever, chills</td>
<td>Initial tests are nonspecific; serology can confirm at four to six weeks</td>
<td>Amoxicillin</td>
</tr>
<tr>
<td><em>Borrelia burgdorferi</em></td>
<td></td>
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<tr>
<td><strong>Human monocytic ehrlichiosis</strong></td>
<td>South, Southeast and Midwest</td>
<td>Fever, chills, headache, myalgias</td>
<td>Leukopenia, thrombocytopenia, elevated liver transaminases; serology can confirm at one to two weeks</td>
<td>Doxycycline Chloramphenicol (Chloromycetin) Rifampin (Rifadin)</td>
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<tr>
<td><em>Ehrlichia chaffeensis</em></td>
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<td><em>Ehrlichia ewingii</em></td>
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<tr>
<td><strong>Human granulocytic ehrlichiosis</strong></td>
<td>Northeast and upper Midwest</td>
<td>Fever, chills, headache, myalgias</td>
<td>Leukopenia, thrombocytopenia, elevated liver transaminases; serology can confirm at one to two weeks</td>
<td>Doxycycline Chloramphenicol Rifampin</td>
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<tr>
<td><em>Ehrlichia phagocytophila/eqi</em></td>
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<tr>
<td><strong>Rocky Mountain spotted fever</strong></td>
<td>Southeast Atlantic coast states and Midwest</td>
<td>Fever, headache, myalgias, malaise, vomiting, rash</td>
<td>Mild leukopenia, thrombocytopenia, elevated liver transaminases, hyponatremia; serology can confirm at seven to 10 days</td>
<td>Tetracycline Chloramphenicol Doxycycline</td>
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<tr>
<td><em>Rickettsia rickettsii</em></td>
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<td></td>
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<tr>
<td><strong>Tularemia</strong></td>
<td>South and Midwest</td>
<td>Fever, chills, headache, malaise, fatigue, cough, myalgias, vomiting, sore throat, abdominal pain, diarrhea, skin ulcers, lymphadenopathy</td>
<td>Normal or slightly elevated white blood cell count and erythrocyte sedimentation rate; serology can confirm at about two weeks</td>
<td>Streptomycin Gentamicin Tetracycline Chloramphenicol Fluoroquinolones</td>
</tr>
</tbody>
</table>
Regional or generalized adenopathy, conjunctivitis, iritis, hepatitis, and microscopic hematuria or proteinuria may also be seen.1,3,5

Late Lyme disease is most often characterized by chronic arthritis. This occurs in about 10 percent of patients with untreated erythema migrans. It is described as a mono- or asymmetric oligoarticular arthritis involving large joints, most often the knee. The neurologic system may also be affected with subacute encephalopathy, axonal polyneuropathy and leukoencephalopathy. The late manifestations generally resolve spontaneously in several years.1,3,5

Lyme disease is diagnosed based on history and physical examination. Routine laboratory tests play only a minor role. Serology is a good confirmatory test, but it is usually not diagnostic until four to six weeks after the onset of symptoms.1 Cerebrospinal fluid (CSF) studies should be obtained if neurologic symptoms are present. Synovial fluid may be obtained if joint involvement occurs to rule out other causes of arthritis.

Early Lyme disease responds well to oral antibiotics, although more severe cases may require parenteral antibiotics. Amoxicillin and doxycycline (Vibramycin) are the drugs of choice with the recommended duration of treatment being two to three weeks.1,5

In 1998, the U.S. Food and Drug Administration approved the first vaccine for the prevention of Lyme disease. Two studies of the recombinant OspA (LYMErix) vaccine have shown it to be 76 to 92 percent effective at preventing symptomatic infections. The Advisory Committee on Immunization Practices recommends that the vaccine should be considered for individuals in high- or moderate-risk areas who have frequent or prolonged exposure to tick-infested habitats. The vaccine may be considered for those who have less exposure to tick-infested habitats in high- or moderate-risk areas. It is not recommended for persons who reside, work or recreate in areas of low or no risk. The vaccine is not recommended for individuals younger than 15 or older than 70 years or for pregnant women because of a lack of studies in these populations.6

**Ehrlichiosis**

Ehrlichiosis is an infectious disease caused by Ehrlichia, which are small, gram-negative, pleomorphic, obligate intracellular organisms. There are two distinct forms of the disease in the United States, human monocytic ehrlichiosis (HME) caused by *Ehrlichia chaffeensis* and *Ehrlichia ewingii*, and human granulocytic ehrlichiosis (HGE) caused by an as yet unnamed species of Ehrlichia, tentatively named *Ehrlichia phagocytophila/Ehrlichia equi*.7

The first report of Ehrlichia disease came in 1935 and occurred in a group of research dogs. In 1986, ehrlichiosis was first identified in humans in the western hemisphere with the organisms found in human monocytes. *E. chaffeensis* was identified as the agent of HME in 1991. Shortly thereafter, a similar illness was identified with Ehrlichia found in polymorphonucleocytes. This disease was later called HGE. The organism responsible was shown to be similar to *E. equi* and *E. phagocytophila*, both known to cause disease in horses and ruminants but not in humans, but the organism has yet to be fully identified.7,8

Ehrlichiosis occurs worldwide, but the majority of cases have been reported in the United States. State health departments reported 364 cases in 1997, but it is not a reportable condition in all states. Overall, HME has a higher incidence than HGE, but this may be affected by reporting bias.7 The highest incidence of HME occurs in the Southeast and Midwest, and the highest incidence of HGE occurs in the Northeast and upper Midwest.9 Most cases of HME and
HGE appear between April and September; more than 75 percent of cases are in men, and older persons are affected more often.

Clinically, HME and HGE are similar, especially initially. Both have incubation periods of about seven to 10 days. Patients usually present with fever, headache, myalgias and shaking chills. Less common symptoms include nausea, vomiting, abdominal pain, diarrhea, cough and confusion. A rash occurs in fewer than one half of patients with HME and fewer than one tenth of those with HGE. The rash involves the trunk, spares the hands and feet and is not associated with the site of the tick bite. It is described variously as macular, papular, reticular, maculopapular and petechial. Complications are more common in HGE and may include respiratory or renal failure, opportunistic infections or hemorrhage (DIC).2,8

The hallmark laboratory features of the disease include leukopenia, thrombocytopenia and elevated liver transaminases. Other possible laboratory findings include a mild transient anemia in HGE, elevated erythrocyte sedimentation rate (ESR), blood urea nitrogen and creatinine in HGE and HME, and CSF with a lymphocytic pleocytosis and elevated protein in HME.8

The diagnosis of ehrlichiosis is based on history, physical examination and the common laboratory findings. Serology is a good confirmatory test but is usually only positive after one or two weeks. Polymerase chain reaction testing is a good confirmatory tool that is useful in the acute setting if it is available to the physician. Culture of the organisms is not practical.

Doxycycline (Vibramycin) is the drug of choice for treatment of ehrlichiosis. Chloramphenicol (Chloromycetin) and rifampin (Rifadin) are alternative treatments. Most recommend treatment for at least two weeks.

Rocky Mountain Spotted Fever

_Rickettsia rickettsii_ is the organism responsible for Rocky Mountain spotted fever. It is a small, pleomorphic, obligate intracellular parasite that infects the endothelial and smooth muscle cells of blood vessels.1 The disease was first described in the northwest United States in the late 19th century. Howard Ricketts identified the causative agent in the early 1900s.9

Rocky Mountain spotted fever is endemic in North, Central, and South America. Three hundred and sixty-five cases were reported to the CDC in 1998. Most cases in the United States occur in the southeast Atlantic coast states and in the Midwest. There is a bimodal age distribution of cases with peaks in children five to nine years of age and adults older than 60 years.9

The incubation period for the disease averages about seven days. Patients present with fever, headache, myalgias, malaise and vomiting. A rash usually occurs within the first week of the illness, described initially as blanching 1- to 4-mm macules that later become petechiae. The rash begins on the wrists and ankles, then spreads to the trunk, palms and soles. About 10 percent of patients do not have a rash.1 The percentage of patients exhibiting the classic triad of fever, rash and tick exposure varies from 3 to 70 percent.1,10

Initial laboratory tests often reveal a normo or slightly depressed white blood cell (WBC) count, thrombocytopenia, elevated liver transaminases and hyponatremia. The CSF may show an increased WBC count with a predominance of monocytes.10

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Major complications include encephalitis, noncardiogenic pulmonary edema, acute respiratory distress syndrome, various cardiac arrhythmias, coagulopathies, gastrointestinal bleeding and skin necrosis. If left untreated, death may occur in eight to 15 days. The mortality rate is reported at 25 percent in untreated cases and 5 percent in treated cases.\(^9\)

Diagnosis is based on history and physical examination. If a rash is present, direct immunofluorescence or immunoperoxidase staining may detect rickettsial organisms within the vascular endothelium of skin biopsies.\(^1\) This method, however, is not commonly used. Serology can be used to confirm the diagnosis, but it is usually not positive until seven to 10 days after the onset of symptoms.

Tetracycline and chloramphenicol are effective treatments. Doxycycline should be the first-line choice according to some individuals. Treatment should be continued for at least five to seven days or until the patient has been afebrile for at least two days.\(^1,3\)

**Tularemia**

Tularemia is an infectious disease caused by *Francisella tularensis*, a small, gram-negative, nonmotile coccobacillus. Several possible modes of transmission to humans exist. Tick bites are thought to account for more than one half of all cases in the United States.\(^1,11\) There has been renewed interest in tularemia in recent years, and the CDC reinstated it as a reportable condition in 2000 because of its potential as a bioterrorism agent.

About 150 to 300 cases are reported each year in the United States. Arkansas, Missouri and Oklahoma account for greater than 50 percent of cases annually.\(^1\) The disease is more common in men, and the peak times of year for the disease are in the summer and fall.\(^1,12\)

The incubation period averages about three to five days. Most patients exhibit generalized symptoms including fever, chills, headache, malaise, anorexia, fatigue, cough, myalgias, chest discomfort, vomiting, sore throat, abdominal pain and diarrhea. In addition to these symptoms, each patient will present with one of six classic patterns of disease.

The ulceroglandular pattern is the most common and easily recognizable. These patients exhibit enlarged, localized, tender lymphadenopathy with a painful skin ulcer in an area draining into the involved lymph nodes. The most common nodes involved are cervical and occipital nodes in children and inguinal nodes in adults. The glandular type of disease is similar, but has no skin ulcer.

In the oculoglandular type, organisms have gained entry through the conjunctiva. Unilateral involvement occurs in 90 percent of cases. Early symptoms include photophobia and increased lacrimation. Later, patients develop lid edema, painful conjunctivitis with scleral injection, chemosis and small yellowish conjunctival ulcers or papules. Preauricular, submandibular and cervical nodes are commonly involved.

In the pharyngeal type, organisms have gained entry through the oropharynx. The predominant complaint is severe sore throat. Examination shows an exudative pharyngitis or tonsillitis and cervical, pre-parotid, or retropharyngeal lymphadenopathy. The typhoidal pattern is not associated with any predominant lymphadenopathy. Symptoms include the common generalized symptoms mentioned above and profuse watery diarrhea.

The pneumonic type of tularemia presents as an acute respiratory illness. Symptoms include fever, cough with minimal or no sputum production, substernal chest tightness and pleuritic chest pain. Chest radiograph may reveal lobar, apical or hilar infiltrates, hilar adenopathy and pleural effusions.\(^1,12\)
Tick-borne Disease

The diagnosis is based on history and physical examination. Common laboratory tests are usually nonspecific. WBC and ESR levels may be normal or slightly elevated. The organism can be cultured, but this is not often done because of the risk of transmission to laboratory workers. Serology can confirm the diagnosis at about two weeks.\textsuperscript{1,12}

Streptomycin is the drug of choice unless meningitis is present. Gentamicin, tetracycline, chloramphenicol and fluoroquinolones are alternative treatments. Therapy is recommended for seven to 14 days.\textsuperscript{12} A live vaccine is available and may be considered for laboratory workers or anyone with repeated exposures.\textsuperscript{1}

**Prevention of Tick-borne Diseases**

The best method of limiting tick-borne diseases is preventing tick bites. Areas where ticks are prevalent including wooded, brushy areas should be avoided. Tick repellants are effective and safe if used correctly. Repellants containing N,N diethyl-m-toluamide (DEET) may be applied to clothing or directly to the skin; those containing permethrin should only be applied to clothing. Wearing long-sleeved shirts and long pants and tucking the pant legs into socks can make ticks more detectable prior to attachment. A careful check of the entire skin surface for ticks following any outdoor activity and the prompt removal of any that are found attached is the best method of preventing the adverse outcomes of tick exposure. Because several hours of tick attachment are thought to be required for transmission of most of these diseases, the more quickly ticks are removed the less chance there is of transmission.\textsuperscript{1}

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