in some U.S. regions. Most *E. chaffeensis* infections are identified in the south-central, southeastern, and mid-Atlantic states, but cases have also been recognized in California and New York. All stages of the Lone Star tick (*A. americanum*) feed on white-tailed deer—a major reservoir. Dogs and coyotes also serve as reservoirs and often lack clinical signs. Tick bites and exposures are frequently reported by patients in rural areas, especially in May through July. The median age of HME patients is 52 years; however, severe and fatal infections in children also are well recognized. Of patients with HME, 60% are male.

E. chaffeensis has been detected in South America, Africa, and Asia.

Clinical Manifestations *E. chaffeensis* disseminates hematogenously from the dermal blood pool created by the feeding tick. After a median incubation period of 8 days, illness develops. Clinical manifestations are undifferentiated and include fever (96% of cases), headache (72%), myalgia (68%), and malaise (77%). Less frequently observed are nausea, vomiting, and diarrhea (25–57%); cough (28%); rash (26% overall, 6% at presentation); and confusion (20%). HME can be severe: 49% of patients with documented cases are hospitalized, and ~2% die. Severe manifestations include a toxic shock–like or septic shock–like syndrome, adult respiratory distress syndrome, cardiac failure, hepatitis, meningoencephalitis, hemorrhage, and—in immunocompromised patients—overwhelming ehrlichial infection. Laboratory findings are valuable in the differential diagnosis of HME; 61% of patients have leukopenia (initially lymphopenia, later neutropenia), 73% have thrombocytopenia, and 84% have elevated serum levels of hepatic aminotransferases. Despite low blood cell counts, the bone marrow is hypercellular, and noncaseating granulomas can be present. Vasculitis is not a component of HME.

Diagnosis HME can be fatal. Early empirical antibiotic therapy based on clinical diagnosis diminishes adverse outcomes. This diagnosis is suggested by fever with a known tick exposure during the preceding 3 weeks, thrombocytopenia and/or leukopenia, and increased serum aminotransferase levels. Morulae are demonstrated in <10% of peripheral-blood smears. HME can be confirmed during active infection by PCR amplification of *E. chaffeensis* nucleic acids in blood obtained before the start of doxycycline therapy. Retrospective serodiagnosis requires a consistent clinical picture and a fourfold increase in *E. chaffeensis* antibody titer to ≥64 in paired sera obtained ~3 weeks apart. Separate specific diagnostic tests are necessary for HME and HGA.

EWINGII EHRLICHIOSIS AND *EHRLICHIA MURIS*–LIKE INFECTIONS

Ehrlichia ewingii, originally a neutrophil pathogen causing fever and lameness in dogs, resembles *E. chaffeensis* in its tick vector (*A. americanum*) and vertebrate reservoirs (white-tailed deer and dogs). An *E. muris*–like agent (EMLA) has been discovered and identified as the cause of human infections in Wisconsin and Minnesota. *E. ewingii* and EMLA illnesses are similar to but less severe than HME. Many cases occur in immunocompromised patients. No specific serologic diagnostic tests for ewingii or EMLA ehrlichiosis are readily available.

CANDIDATUS NEOEHRLICHIA MIKURENSIS INFECTION

Candidatus Neoehrlichia mikurensis, a bacterium in a phylogenetic clade between *Ehrlichia* and *Anaplasma*, was originally identified in *Ixodes ricinus* ticks from the Netherlands and in mice and *Ixodes ovatus* ticks from Japan. By means of broad-range 16S rRNA gene amplification and sequence analysis, this organism was identified as the cause of severe and sometimes prolonged febrile illnesses in European immunocompromised patients with tick bites or exposures and in Chinese patients with a mild febrile illness after being bitten by *Ixodes persulcatus* and *Haemaphysalis concinna* ticks. The clinical presentation is similar to those of HME and HGA. Specific diagnostic methods have been developed but are not widely available.

TREATMENT **EHRLICHIOSES**

Doxycycline is effective for HME as well as for ewingii and EMLA ehrlichioses; the use of this drug in *Candidatus* N. mikurensis infection is associated with disease resolution. Therapy with doxycycline (100 mg given PO or IV twice daily) or tetracycline (250–500 mg given PO every 6 h) lowers hospitalization rates and shortens fever duration. *E. chaffeensis* is not susceptible to chloramphenicol in vitro, and the use of this drug is controversial. While a few reports document *E. chaffeensis* persistence in humans, this finding is rare; most infections are cured by short courses of doxycycline (continuing for 3–5 days after defervescence). Although poorly studied, rifampin may be suitable when doxycycline is contraindicated.

PREVENTION

HME, ewingii ehrlichiosis, EMLA infection, and *Candidatus* N. mikurensis infection can be prevented by the avoidance of ticks in endemic areas. The use of protective clothing and tick repellents, careful post-exposure tick searches, and prompt removal of attached ticks probably diminish infection risk.

HUMAN GRANULOCYTOTROPIC ANAPLASMOSIS

Epidemiology As of April 2013, 10,181 cases of HGA had been reported to the CDC, most in the upper midwestern and northeastern United States; the geographic distribution is similar to that for Lyme disease because of the shared *I. scapularis* tick vector. White-footed mice, squirrels, and white-tailed deer in the United States and red deer in Europe are natural reservoirs for *A. phagocytophilum*. HGA incidence peaks in May through July, but the disease can occur throughout the year with exposure to *Ixodes* ticks. HGA often affects males (59%) and older persons (median age, 51 years).

Clinical Manifestations Seroprevalence rates are high in endemic regions; thus it seems likely that most individuals develop subclinical infections. The incubation period for HGA is 4–8 days, after which the disease manifests as fever (75–100% of cases), myalgia (77%), headache (82%), and malaise (97%). A minority of patients develop nausea, vomiting, or diarrhea (22–39%); cough (27%); or confusion (17%). Rash (6%) is almost invariably concurrent erythema migrans attributable to Lyme disease. Most patients develop thrombocytopenia (75%) and/or leukopenia (55%) with increased serum hepatic aminotransferase levels (83%).

Severe complications occur most often in the elderly and include adult respiratory distress syndrome, a toxic shock–like syndrome, and life-threatening opportunistic infections. Meningoencephalitis is rarely documented with HGA, but brachial plexopathy, cranial nerve involvement, and demyelinating polyneuropathy are reported. For HGA, 7% of patients require intensive care, and the case-fatality rate is 0.6%. Neither vasculitis nor granulomas are components of HGA. While co-infections with *Borrelia burgdorferi* and *Babesia microti* (transmitted by the same tick vector[s]) occur, there is little evidence of comorbidity or persistence. HGA is rarely acquired via transfusion.

Diagnosis HGA should be included in the differential diagnosis of influenza-like illnesses during seasons with *Ixodes* tick activity (May through December), especially with known tick bite or exposure. Concurrent thrombocytopenia, leukopenia, or elevated serum levels of alanine or aspartate aminotransferase further increase the likelihood of HGA. Many HGA patients develop Lyme disease antibodies in the absence of clinical findings consistent with that diagnosis. Thus, HGA should be considered in the differential diagnosis of atypical severe Lyme disease presentations. Peripheral-blood film examination for neutrophil morulae can yield a diagnosis in 20–75% of infections. PCR testing of blood from patients with active disease before doxycycline therapy is sensitive and specific. Serodiagnosis is retrospective, requiring a fourfold increase in *A. phagocytophilum* antibody titer (to ≥160) in paired serum samples obtained 1 month apart. Since seroprevalence is high in some regions, a single acute-phase titer should not be used for diagnosis.