



Murine typhus is a worldwide illness caused by *Rickettsia typhi* organisms that are transmitted by fleas. It produces a moderately severe illness characterized by fever, rash, and headache. Disease in the United States has been reported in Texas and Southern California.

*Rickettsia africae*, the cause of African tick-bite fever, occurs in travelers returning from East Africa. It produces a large eschar with a febrile syndrome similar to RMSF. Rickettsial infections respond to treatment with doxycycline and warrant rapid initiation of treatment.

### Lyme Disease

Lyme disease is a tick-borne illness caused by pathogenic species of the spirochete *Borrelia burgdorferi* in the United States. Other species in Europe and Asia can cause more aggressive presentations. Localized disease includes erythema migrans in 80% of patients and nonspecific findings that resemble a viral syndrome. Erythema migrans is an expanding macule that forms an annular lesion with a clearing middle.

Early disseminated Lyme disease with acute neurologic or cardiac involvement usually occurs weeks to several months after the tick bite and may be the first manifestation of the disease. Nonspecific symptoms (e.g., headache, fatigue, arthralgias) may persist for months after treatment of Lyme disease. There is no evidence that these persistent subjective complaints represent ongoing active infection. Co-infection with *Babesia* and *Ehrlichia* is common, and these infections should be considered in persons diagnosed with Lyme disease.

### Human Ehrlichiosis

The principal vector of *Ehrlichia chaffeensis*, the agent that causes human monocytic ehrlichiosis (HME), is the Lone Star tick (*Amblyomma americanum*). Patients typically have an acute illness that has an incubation period of 1 to 2 weeks. Most patients are febrile and have nonspecific symptoms such as malaise, myalgia, headache, and chills.

One feature that may distinguish HME from human granulocytic anaplasmosis (HGA), another tick-borne illness caused by *Anaplasma phagocytophilum*, is a rash (macular, maculopapular, or petechial). This rash occurs in about 30% of patients with HME but is rare in patients with HGA.

The preferred and most widely available diagnostic method for ehrlichiosis is the indirect fluorescent antibody test. The diagnosis should be considered in all patients with Lyme disease or babesiosis. Treatment with doxycycline should be initiated for all patients suspected of having ehrlichiosis or anaplasmosis.

### Viral Infections Associated with Rash

The typical manifestations of viral infections associated with rash may unequivocally establish the cause of a febrile syndrome. For example, varicella-zoster virus infection manifests with distinctive lesions of chickenpox or herpes zoster (i.e., shingles). The resurgence of measles mandates the ability to recognize its rash.

Acute onset of high fever characterizes viral hemorrhagic fevers, along with bleeding complications and high mortality rates in some cases. Arthropods often transmit viral infections, including dengue, which is one of the most common causes of fever in returned travelers. The deer tick virus identified in New

York State causes a syndrome of fever and confusion with or without rash.

### Fever with Lymphadenopathy

Generalized and localized lymphadenopathy can be major manifestations of some infectious diseases, such as in mononucleosis syndromes, tuberculosis, HIV infection, and pyogenic infections.

Infectious mononucleosis is characterized by a triad of fever, tonsillar pharyngitis, and lymphadenopathy. EBV is a widely disseminated herpesvirus that is spread by intimate contact between susceptible persons and EBV shedders. Lymph node involvement in infectious mononucleosis is typically symmetrical and more commonly involves the posterior cervical than the anterior chains. The posterior cervical nodes are deep beneath the sternocleidomastoid muscles and must be carefully palpated. The nodes may be large and moderately tender. Lymphadenopathy may also become more generalized including enlargement of the spleen, which distinguishes infectious mononucleosis from other causes of pharyngitis.

Lymphadenopathy peaks in the first week and then gradually subsides over 2 to 3 weeks. Splenomegaly is seen in 50% of patients with infectious mononucleosis and usually begins to recede by the third week of the illness.

Patients with a clinical picture of infectious mononucleosis should have a white blood cell count with differential and a heterophile (Monospot) test. If the heterophile test result is positive, no further testing is necessary when the clinical scenario is compatible with typical infectious mononucleosis. If the heterophile test result is negative but there is still a strong clinical suspicion of EBV infection, the Monospot test can be repeated because results can be negative early in clinical illness.

If the clinical syndrome is prolonged or the patient does not have a classic EBV syndrome, immunoglobulin M (IgM) and immunoglobulin G (IgG) viral capsid antigen (VCA) and Epstein-Barr nuclear antigen (EBNA) antibodies should be measured. IgG EBNA detected within 4 weeks of symptom onset excludes acute primary EBV infection as an explanation and should prompt consideration of EBV-negative causes of mononucleosis.

### Cytomegalovirus

The spectrum of human illness caused by CMV is diverse and mostly depends on the host. CMV infection in the immunocompetent host usually is asymptomatic or may manifest as a mononucleosis-like syndrome. Transmission occurs through multiple routes.

The mononucleosis syndrome associated with CMV infection has been described as typhoidal because systemic symptoms and fever predominate, and signs of enlarged cervical nodes and splenomegaly are not as commonly seen as they are in EBV infection. Diarrhea, fever, fatigue, and abdominal pain are common symptoms. Immunocompromised patients, such as those who have received transplants, may have serious, life-threatening infections such as pneumonitis, hepatitis, colitis, and retinitis. Serology provides indirect evidence of recent CMV infection based on changes in antibody titers at different time points during the