



organism infects rodents, cattle, swine, dogs, horses, sheep, and goats, and it is shed in the urine. Humans most often become infected after exposure to environmental sources, such as contaminated water.

Leptospirosis may manifest as a subclinical illness followed by seroconversion, a self-limited systemic infection, or a severe, potentially fatal illness accompanied by multiorgan failure. Acute illness manifests with the abrupt onset of fever, rigors, myalgias, and headache in 75% to 100% of patients. Conjunctival suffusion in a patient with a nonspecific febrile illness accompanied by lymphadenopathy, hepatomegaly, and splenomegaly points to a diagnosis of leptospirosis.

During the second phase of illness, fever is less pronounced, but headache and myalgias can be severe, and aseptic meningitis is an important manifestation. In some patients with leptospirosis, the clinical course may be complicated by jaundice (although liver failure is rare), renal failure, uveitis, hemorrhage, ARDS, myocarditis, and rhabdomyolysis (i.e., Weil's syndrome).

Because the clinical features and routine laboratory findings of leptospirosis are not specific, a high index of suspicion must be maintained. The diagnosis is usually made by serologic testing for *L. interrogans*. Symptomatic individuals warrant treatment with doxycycline.

Brucellosis

Brucellosis is a zoonotic infection caused by *Brucella melitensis*. It is transmitted to humans by contact with fluids from infected animals (i.e., sheep, cattle, goats, pigs, or other animals) or derived food products such as unpasteurized milk and cheese.

Clinical manifestations of brucellosis include fever, night sweats, malaise, anorexia, arthralgias, fatigue, weight loss, and depression. Patients may have fever and a multitude of complaints but no other objective findings. The onset of symptoms may be abrupt or insidious, developing over several days to weeks. The musculoskeletal and genitourinary systems are the most common sites of involvement. Neurobrucellosis, endocarditis, and hepatic abscesses occur in 1% to 2% of cases.

The diagnosis of brucellosis should be considered for an individual with otherwise unexplained fever and nonspecific complaints who has had a possible exposure. Ideally, the diagnosis is made by culture of the organism from blood or other sites, such as bone marrow. Serologic tests include tube agglutination and enzyme-linked immunosorbent assay (ELISA). For adults with nonfocal disease, treatment with doxycycline and rifampin is suggested.

Fever and Rash

The most concerning diseases associated with fever and rash are meningococemia, staphylococcal TSS, and RMSF.

Bacterial Meningitis

Neisseria meningitidis is the leading cause of bacterial meningitis in children and young adults in the United States. Recent experience in New York City identified HIV patients as being at increased risk for meningococcal disease.

Manifestations of meningococcal disease can range from transient fever and bacteremia to fulminant disease, with death ensuing within hours of the onset of clinical symptoms. Acute

systemic meningococcal disease may manifest as one of three syndromes: meningitis alone, meningitis with accompanying meningococemia, and meningococemia without clinical evidence of meningitis.

The typical initial symptoms of meningitis due to *N. meningitidis* consists of the sudden onset of fever, nausea, vomiting, headache, decreased ability to concentrate, and myalgias in an otherwise healthy patient. A petechial rash appears as discrete lesions 1 to 2 mm in diameter, most frequently occurring on the trunk and lower portions of the body. More than 50% of patients have petechiae at clinical presentation. Petechiae can coalesce into larger purpuric and ecchymotic lesions.

Staphylococcal Toxic Shock Syndrome

S. aureus strains produce exotoxins that cause three syndromes: food poisoning, caused by ingestion of *S. aureus* enterotoxin; scalded skin syndrome, caused by exfoliative toxin; and TSS, caused by toxic shock syndrome toxin 1 (TSST-1) and other enterotoxins. About one half of reported TSS cases are menstrual, associated with bacterial growth on highly absorbent tampons. Nonmenstrual TSS has been associated with surgical and postpartum wound infections, mastitis, septorhinoplasty, sinusitis, osteomyelitis, arthritis, burns, cutaneous and subcutaneous lesions (especially of the extremities, perianal area, and axillae), and respiratory infections after influenza. Some MRSA strains can produce TSST-1, and patients infected with these strains may develop TSS.

The Centers for Disease Control and Prevention (CDC) case definition for a confirmed case includes several criteria. Patients must have fever greater than 38.9° C, hypotension, diffuse erythroderma, desquamation (unless the patient dies before desquamation can occur), and involvement of at least three organ systems. Although 80% to 90% of TSS patients have *S. aureus* isolated from mucosal or wound sites, the isolation of *S. aureus* is not required for the diagnosis of staphylococcal TSS.

Rickettsial Infections

RMSF is a potentially lethal but usually curable tick-borne disease. Most cases of RMSF occur in the spring and early summer in endemic areas, particularly in the south central and southeastern states, when outdoor activity is most common. The etiologic agent, *Rickettsia rickettsii*, is a gram-negative, obligate intracellular bacterium that is usually transmitted through a tick bite. Up to one third of patients with proven RMSF do not recall a recent tick bite or recent tick contact.

In the early phases of illness, most patients have nonspecific signs and symptoms such as fever, headache, malaise, myalgias, arthralgias, and nausea with or without vomiting. Most patients with RMSF develop a rash between the third and fifth days of illness. The rash typically begins with pink, blanching macules that evolve to a deep red color and then become hemorrhagic. The lesions begin at the wrists, forearms, and ankles and then spread to the arms, thighs, trunk, and face.

The diagnosis of RMSF is based on a constellation of symptoms and signs in an appropriate epidemiologic setting (e.g., endemic area in the spring or early summer). In later illness, the diagnosis can be made by skin biopsy and confirmed serologically.