FIGURE 211-1 ***Top:*** Petechial lesions of Rocky Mountain spotted fever on the lower legs and soles of a young, previously healthy patient. ***Bottom:*** Close-up of lesions from the same patient. *(Photos courtesy of Dr. Lindsey Baden; with permission.)*

the course (after day 5 in 43% of cases) and does not develop at all in 18–64% of cases.

Hypovolemia leads to prerenal azotemia and (in 17% of cases) hypotension. Infection of the pulmonary microcirculation leads to noncardiogenic pulmonary edema; 12% of patients have severe respiratory disease, and 8% require mechanical ventilation. Cardiac involvement manifests as dysrhythmia in 7–16% of cases.

Besides respiratory failure, central nervous system (CNS) involvement is the other important determinant of the outcome of RMSF. Encephalitis, presenting as confusion or lethargy, is apparent in 26–28% of cases. Progressively severe encephalitis manifests as stupor or delirium in 21–26% of cases, ataxia in 18%, coma in 10%, and seizures in 8%. Numerous focal neurologic deficits have been reported. Meningoencephalitis results in cerebrospinal fluid (CSF) pleocytosis in 34–38% of cases; usually there are 10–100 cells/μL and a mononuclear predominance, but occasionally there are >100 cells/μL and a polymorphonuclear predominance. The CSF protein concentration is increased in 30–35% of cases, but the CSF glucose concentration is usually normal.

Renal failure, often reversible with rehydration, is caused by acute tubular necrosis in severe cases with shock. Hepatic injury with increased serum aminotransferase concentrations (38% of cases) is due to focal death of individual hepatocytes without hepatic failure. Jaundice is recognized in 9% of cases and an elevated serum bilirubin concentration in 18–30%.

Life-threatening bleeding is rare. Anemia develops in 30% of cases and is severe enough to require transfusions in 11%. Blood is detected in the stool or vomitus of 10% of patients, and death has followed massive upper-gastrointestinal hemorrhage.

Other characteristic clinical laboratory findings include increased plasma levels of proteins of the acute-phase response (C-reactive

protein, fibrinogen, ferritin, and others), hypoalbuminemia, and hyponatremia (in 56% of cases) due to the appropriate secretion of antidiuretic hormone in response to the hypovolemic state. Myositis occurs occasionally, with marked elevations in serum creatine kinase levels and multifocal rhabdomyonecrosis. Ocular involvement includes conjunctivitis in 30% of cases and retinal vein engorgement, flame hemorrhages, arterial occlusion, and papilledema with normal CSF pressure in some instances.

In untreated cases, the patient usually dies 8–15 days after onset. A rare presentation, fulminant RMSF, is fatal within 5 days after onset. This fulminant presentation is seen most often in male black patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency and may be related to an undefined effect of hemolysis on the rickettsial infection. Although survivors of RMSF usually return to their previous state of health, permanent sequelae, including neurologic deficits and gangrene necessitating amputation of extremities, may follow severe illness.

Diagnosis The diagnosis of RMSF during the acute stage is more difficult than is generally appreciated. The most important epidemiologic factor is a history of exposure to a potentially tick-infested environment within the 14 days preceding disease onset during a season of possible tick activity. However, only 60% of patients actually recall being bitten by a tick during the incubation period.

The differential diagnosis for early clinical manifestations of RMSF (fever, headache, and myalgia without a rash) includes influenza, enteroviral infection, infectious mononucleosis, viral hepatitis, leptospirosis, typhoid fever, gram-negative or gram-positive bacterial sepsis, HME, HGA, murine typhus, sylvatic flying-squirrel typhus, and rickettsialpox. Enterocolitis may be suggested by nausea, vomiting, and abdominal pain; prominence of abdominal tenderness has resulted in exploratory laparotomy. CNS involvement can masquerade as bacterial or viral meningoencephalitis. Cough, pulmonary signs, and chest radiographic opacities can lead to a diagnostic consideration of bronchitis or pneumonia.

At presentation during the first 3 days of illness, only 3% of patients exhibit the classic triad of fever, rash, and history of tick exposure. When a rash appears, a diagnosis of RMSF should be considered. However, many illnesses considered in the differential diagnosis also can be associated with a rash, including rubeola, rubella, meningococcemia, disseminated gonococcal infection, secondary syphilis, toxic shock syndrome, drug hypersensitivity, idiopathic thrombocytopenic purpura, thrombotic thrombocytopenic purpura, Kawasaki syndrome, and immune complex vasculitis. Conversely, any person in an endemic area with a provisional diagnosis of one of the above illnesses could have RMSF. Thus, if a viral infection is suspected during RMSF season in an endemic area, it should always be kept in mind that RMSF can mimic viral infection early in the course; if the illness worsens over the next couple of days after initial presentation, the patient should return for reevaluation.

The most common serologic test for confirmation of the diagnosis is the indirect immunofluorescence assay. Not until 7–10 days after onset is a diagnostic titer of ≥64 usually detectable. The sensitivity and specificity of the indirect immunofluorescence IgG assay are 89–100% and 99–100%, respectively. It is important to understand that serologic tests for RMSF are usually negative at the time of presentation for medical care and that treatment should not be delayed while a positive serologic result is awaited.

The only diagnostic test that has proven useful during the acute illness is immunohistologic examination of a cutaneous biopsy sample from a rash lesion for *R. rickettsii*. Examination of a 3-mm punch biopsy from such a lesion is 70% sensitive and 100% specific. The sensitivity of polymerase chain reaction (PCR) amplification and detection of *R. rickettsii* DNA in peripheral blood is improving. However, although rickettsiae are present in large quantities in heavily infected foci of endothelial cells, there are relatively low quantities in the circulation. Cultivation of rickettsiae in cell culture is feasible but is seldom undertaken because of biohazard concerns. The recent dramatic increase in the reported incidence of RMSF correlates with