A. aegypti exist in Hawaii and the southern United States. The range of a lesser dengue virus vector, *A. albopictus*, now extends from Asia to the United States, the Indian Ocean, parts of Europe, and Hawaii. *A. aegypti* typically breeds near human habitation, using relatively fresh water from sources such as water jars, vases, discarded containers, coconut husks, and old tires. The mosquito usually inhabits dwellings and bites during the day. Bursts of dengue cases are to be expected in the southern United States, particularly along the Mexican border, where containers of water may be infested with *A. aegypti*. Closed habitations with air-conditioning may inhibit transmission of many arboviruses, including dengue viruses 1–4.

Dengue begins after an incubation period averaging 4–7 days, when the typical patient experiences the sudden onset of fever, frontal headache, retroorbital pain, and back pain along with severe myalgias. These symptoms gave rise to the colloquial designation of dengue as "break-bone fever." Often a transient macular rash appears on the first day, as do adenopathy, palatal vesicles, and scleral injection. The illness may last a week, with additional symptoms and clinical signs usually including anorexia, nausea or vomiting, and marked cutaneous hypersensitivity. Near the time of defervescence on days 3–5, a maculopapular rash begins on the trunk and spreads to the extremities and the face. Epistaxis and scattered petechiae are often noted in uncomplicated dengue, and preexisting gastrointestinal lesions may bleed during the acute illness.

Laboratory findings of dengue include leukopenia, thrombocytopenia, and, in many cases, elevations of serum aminotransferase concentrations. The diagnosis is made by IgM ELISA or paired serology during recovery or by antigen-detection ELISA or RT-PCR during the acute phase. Virus is readily isolated from blood in the acute phase if mosquito inoculation or mosquito cell culture is used.

Reoviruses Several orbiviruses (Lebombo, Kemerovo, Orungo, and Tribeč viruses) and coltiviruses (Colorado tick fever, Eyach, and Salmon River viruses) can cause fever and myalgia in humans. With the exception of Lebombo and Orungo viruses, all of these viruses are transmitted by ticks. The most important reoviral arthropod-borne disease is Colorado tick fever. Several hundred patients with this disease are reported annually in the United States. The infection is acquired between March and November through the bite of an infected ixodid tick, the Rocky Mountain wood tick (*Dermacentor andersoni*), in mountainous western regions at altitudes of 1200–3000 m. Small mammals serve as amplifying hosts. The most common presentation is fever and myalgia; meningoencephalitis is not uncommon, and hemorrhagic disease, pericarditis, myocarditis, orchitis, and pulmonary presentations have also been reported. Rash develops in a minority of patients. Leukopenia and thrombocytopenia are also noted. The disease usually lasts 7–10 days and is often biphasic. The most important differential diagnostic considerations since the beginning of the twentieth century have been Rocky Mountain spotted fever (although Colorado tick fever is much more common in Colorado) and tularemia. Colorado tick fever virus replicates for several weeks in erythropoietic cells and can be found in erythrocytes. This feature, detected in erythroid smears stained by immunofluorescence, can be diagnostically helpful and is important during screening of blood donors.

PULMONARY DISEASE

Hantavirus pulmonary syndrome (HPS) was first described in 1993, but retrospective identification of cases by immunohistochemistry (1978) and serology (1959) support the idea that HPS is a recently discovered rather than a truly new disease. The causative agents are hantaviruses of a distinct phylogenetic lineage that is associated with the cricetid rodent subfamily Sigmodontinae. Sin Nombre virus, which chronically infects North American deer mice (*Peromyscus maniculatus*), is the most important agent of HPS in the United States. Several other related viruses (Anajatuba, Andes, Araraquara, Araucária, Bayou, Bermejo, Black Creek Canal, Blue River, Castelo dos Sonhos, El Moro Canyon, Juquitiba, Laguna Negra, Lechiguanas, Maciel, Monongahela, Muleshoe, New York, Orán, Paranoá, Pergamino, Río Mamoré, and Tunari) cause the disease in North and South America, but Andes virus is unusual in that it has been implicated in human-to-human transmission. HPS particularly affects rural residents living in dwellings permeable to rodent entry or working in occupations that pose a risk of rodent exposure. Each type of rodent has its own particular habits; in the case of deer mice, these behaviors include living in and around human habitation.

HPS begins with a prodrome of ~3–4 days (range, 1–11 days) comprising fever, malaise, myalgia, and—in many cases—gastrointestinal disturbances such as abdominal pain, nausea, and vomiting. Dizziness is common and vertigo occasional. Severe prodromal symptoms/signs may bring some patients to medical attention, but most cases are recognized as the pulmonary phase begins. Typical signs are slightly lowered blood pressure, tachycardia, tachypnea, mild hypoxemia, thrombocytopenia, and early radiographic signs of pulmonary edema. Physical findings in the chest are often surprisingly scant. The conjunctival and cutaneous signs of vascular involvement seen in hantavirus VHFs (see below) are uncommon. During the next few hours, decompensation may progress rapidly to severe hypoxemia and respiratory failure.

The HPS differential diagnosis includes abdominal surgical conditions and pyelonephritis as well as rickettsial disease, sepsis, meningococcemia, plague, tularemia, influenza, and relapsing fever. A specific diagnosis is best made by IgM antibody testing of acute-phase serum, which has yielded positive results even in the prodrome. Tests using a Sin Nombre virus antigen detect antibodies to the related HPS-causing hantaviruses. Occasionally, heterotypic viruses will react only in the IgG ELISA, but such a finding is highly suspicious given the very low seroprevalence of these viruses in normal populations. RT-PCR is usually positive when used to test blood clots obtained in the first 7–9 days of illness and when used to test tissues; this assay is useful in identifying the infecting virus in areas outside the home range of deer mice and in atypical cases.

During the prodrome, the differential diagnosis of HPS is difficult, but by the time of presentation or within 24 h thereafter, a number of diagnostically helpful clinical features become apparent. Cough usually is not present at the outset. Interstitial edema is evident on a chest x-ray. Later, bilateral alveolar edema with a central distribution develops in the setting of a normal-sized heart; occasionally, the edema is initially unilateral. Pleural effusions are often seen. Thrombocytopenia, circulating atypical lymphocytes, and a left shift (often with leukocytosis) are almost always evident; thrombocytopenia is a particularly important early clue. Hemoconcentration, hypoalbuminemia, and proteinuria should also be sought for diagnosis. Although thrombocytopenia virtually always develops and prolongation of the partial thromboplastin time is the rule, clinical evidence for coagulopathy or laboratory indications of disseminated intravascular coagulation (DIC) are found in only a minority of severely ill patients. Patients with severe illness also have acidosis and elevated serum lactate concentrations. Mildly increased values in renal function tests are common, but patients with severe HPS often have markedly elevated serum creatinine concentrations. Some New World hantaviruses other than Sin Nombre virus (e.g., Andes virus) have been associated with more kidney involvement, but few such cases have been studied.

Management of HPS during the first few hours after presentation is critical. The goal is to prevent severe hypoxemia by oxygen therapy, with intubation and intensive respiratory management if needed. During this period, hypotension and shock with increasing hematocrit invite aggressive fluid administration, but this intervention should be undertaken with great caution. Because of low cardiac output with myocardial depression and increased pulmonary vascular permeability, shock should be managed expectantly with pressors and modest infusion of fluid guided by pulmonary capillary wedge pressure. Mild cases can be managed by frequent monitoring and oxygen administration without intubation. Many patients require intubation to manage hypoxemia and developing shock. Extracorporeal membrane oxygenation is instituted in severe cases, ideally before the onset of shock. The procedure is indicated in patients who have a cardiac index of 2.3 L/min/m^2 or an arterial oxygen tension/fractional inspired oxygen (Pa_{O2}/FI_{O2}) ratio of