

Rodent-borne viruses are maintained in nature by transmission between rodents, which become chronically infected. Usually a high degree of rodent–virus specificity is observed, and overt disease in the reservoir host is rare.

## ETIOLOGY

Arthropod-borne and rodent-borne zoonotic viruses belong to at least seven families: Arenaviridae, Bunyaviridae, Flaviviridae, Orthomyxoviridae, Reoviridae, Rhabdoviridae, and Togaviridae (Table 233-1).

### ARENAVIRIDAE

The members of the family Arenaviridae that infect humans are all assigned to the genus *Arenavirus*. The members of this genus are divided into two main phylogenetic branches: Old World viruses (the Lassa–lymphocytic choriomeningitis serocomplex) and New World viruses (the Tacaribe serocomplex). Human arenaviruses form spherical, oval, or pleomorphic enveloped and spiked virions (~50–300 nm in diameter) that bud from the infected cell's plasma membrane. The particles contain two genomic single-stranded RNAs (S, ~3.5 kb; and L, ~7.5 kb) encoding structural proteins in an ambisense orientation. Most arenaviruses persist in nature by chronically infecting rodents. The Old World viruses are maintained by murid rodents that often are persistently viremic and commonly transmit viruses vertically and horizontally. New World viruses are found in cricetid rodents; horizontal transmission is typical, vertical infection may occur, and persistent viremia may be observed. Strikingly, each arenavirus is predominantly adapted to one particular type of rodent. Humans usually become infected through inhalation of or direct contact with infected rodent excreta or secreta (e.g., aerosols of rodents in harvesting machines; aerosolized dried rodent urine or feces in barns or houses; direct contact with rodents in traps). Person-to-person transmission of arenaviruses is uncommon.

### BUNYAVIRIDAE

The family Bunyaviridae includes four medically significant genera: *Hantavirus*, *Nairovirus*, *Orthobunyavirus*, and *Phlebovirus*. The members of all these genera form spherical to pleomorphic enveloped virions containing three genomic single-stranded RNAs (S, ~1–2 kb; M, 3.6–5.3 kb; and L, 6.4–12.3 kb) of negative (hantaviruses, nairoviruses, orthobunyaviruses) or ambisense (nairoviruses) polarity. Bunyaviruses mature into particles ~80–120 nm in diameter in the Golgi complex of infected cells and exit these cells by exocytosis.

Hantaviruses are unique among the bunyaviruses in that they are not transmitted by arthropods but instead are maintained in nature by rodents that chronically shed virions. Old World hantaviruses are harbored by murid and cricetid rodents, and New World hantaviruses are maintained by cricetid rodents. As with arenaviruses, individual hantaviruses usually are specifically adapted to a particular type of rodent. However, hantaviruses do not cause chronic viremia in their rodent hosts and are transmitted only horizontally from rodent to rodent. Similar to arenaviruses, hantaviruses infect humans primarily through inhalation of or direct contact with rodent excreta or secreta, and person-to-person transmission is not a common event (with the notable exception of Andes virus). Although there is overlap, the human Old World hantaviruses usually are the etiologic agents of hemorrhagic fever with renal syndrome, whereas the New World viruses usually cause hantavirus pulmonary syndrome.

Nairoviruses are maintained by ixodid ticks, which vertically (transovarially and transstadially) transmit these viruses to progeny tick generations and horizontally spread them through viremic vertebrate hosts. Humans are usually infected via a tick bite or during handling of infected vertebrates.

Orthobunyaviruses are largely mosquito-borne and rarely midge-borne and have viremic vertebrate intermediate hosts. Many orthobunyaviruses are also transovarially transmitted in their mosquito host. Numerous orthobunyaviruses have been associated with human infection and disease. They have been considered to be members of ~19 serogroups based on antigenic cross-reactions, but this grouping is

currently undergoing revision with the accumulation of new genomic data and phylogenetic analyses. Human viruses are found in at least nine serogroups.

Phleboviruses are transmitted vertically (transovarially) in their arthropod hosts and horizontally through viremic vertebrate hosts. Phleboviruses are divided into two groups: the phlebotomus group viruses are transmitted by sandflies and the Uukuniemi group viruses by ticks. Phleboviruses are assigned to at least 10 serocomplexes; human pathogens are found in at least four of these serocomplexes.

### FLAVIVIRIDAE

The family Flaviviridae currently includes four genera, one of which (*Flavivirus*) comprises arthropod-borne human viruses. Flaviviruses sensu stricto have single-stranded positive-sense RNA genomes (~11 kb) and form spherical enveloped particles 40–60 nm in diameter. The flaviviruses discussed here belong to two phylogenetically and antigenically distinct groups and are transmitted among vertebrates by mosquitoes and ixodid ticks, respectively. Vectors are usually infected when they feed on viremic hosts; as in the case of most other viruses discussed here, humans are accidental hosts who usually are infected by arthropod bites. Arthropods maintain flavivirus infections horizontally, although transovarial transmission has been documented. Under certain circumstances, flaviviruses can also be transmitted by aerosols or via contaminated food products; in particular, raw milk can transmit tick-borne encephalitis virus.

### ORTHOMYXOVIRIDAE

The family Orthomyxoviridae includes two genera of medically relevant arthropod-borne viruses: *Quarantavirus* and *Thogotovirus*. Quarantaviruses are transmitted among birds by ixodid ticks, whereas thogotoviruses have a predilection for mammalian host reservoirs and can be transmitted by both ixodid ticks and mosquitoes.

### REOVIRIDAE

The family Reoviridae contains viruses with linear, multisegmented, double-stranded RNA genomes (~16–29 kb in total). These viruses produce particles that have icosahedral symmetry and are 60–80 nm in diameter. In contrast to all other virions discussed here, reovirions are not enveloped and thus are insensitive to detergent inactivation. Fifteen genera of reoviruses are currently recognized. Human arthropod-borne viruses are found among the genera *Coltivirus* (subfamily Spinareovirinae), *Orbivirus*, and *Seadornavirus* (subfamily Sedoreovirinae). Arthropod-borne coltiviruses possess 12 genome segments. Coltiviruses are transmitted by numerous tick types transstadially but not transovarially. Overall maintenance of the transmission cycle, therefore, involves viremic mammalian hosts infected by tick bites. Arthropod-borne orbiviruses have 10 genome segments and are transmitted by mosquitoes or ixodid ticks, whereas relevant seadornaviruses have 12 genome segments and are transmitted exclusively by mosquitoes.

### RHABDOVIRIDAE

The family Rhabdoviridae is included in the order *Mononegavirales*. Viruses of the nine rhabdovirus genera have linear, nonsegmented, single-stranded RNA genomes of negative polarity (~11–15 kb) and form bullet-shaped to pleomorphic enveloped particles (100–430 nm long and 45–100 nm wide). Only the genus *Vesiculovirus* includes human arthropod-borne viruses, all of which are transmitted by insects (biting midges, mosquitoes, and sandflies). **The general properties of rhabdoviruses are discussed in more detail in Chap. 232.**

### TOGAVIRIDAE

The members of the family Togaviridae have linear, single- and positive-stranded RNA genomes (~9.7–11.8 kb) and form enveloped icosahedral virions (~60–70 nm in diameter) that bud from the plasma membrane of the infected cell. The togaviruses discussed here are all members of the genus *Alphavirus* and are transmitted among vertebrates by mosquitoes.