EPIDEMIOLOGY

Rabies is a zoonotic infection that occurs in a variety of mammals throughout the world except in Antarctica and on some islands. Rabies virus is usually transmitted to humans by the bite of an infected animal. Worldwide, endemic canine rabies is estimated to cause 55,000 human deaths annually. Most of these deaths occur in Asia and Africa, with rural populations and children most frequently affected. Thus, in many resource-poor and resource-limited countries, canine rabies continues to be a threat to humans. However, in Latin America, rabies control efforts in dogs have been quite successful in recent years. Endemic canine rabies has been eliminated from the United States and most other resource-rich countries. Rabies is endemic in wildlife species, and a variety of animal reservoirs have been identified in different countries. Surveillance data from 2012 identified 6162 confirmed animal cases of rabies in the United States (including Puerto Rico). Only 8% of these cases were in domestic animals, including 257 cases in cats, 84 in dogs, and 115 in cattle. In North American wildlife reservoirs, including bats, raccoons, skunks, and foxes, the infection is endemic, with involvement of one or more rabies virus variants in each reservoir species (Fig. 232-1). "Spillover" of rabies to other wildlife species and to domestic animals occurs. Bat rabies virus variants are present in every state except Hawaii and are responsible for most indigenously acquired human rabies cases in the United States. Raccoon rabies is endemic along the entire eastern coast of the United States. Skunk rabies is present in the midwestern states, with another focus in California. Rabies in foxes occurs in Texas, New Mexico, Arizona, and Alaska.

In Canada and Europe, epizootics of rabies in red foxes have been well controlled with the use of baits containing rabies vaccine. A similar approach is used in Canada to control raccoon rabies.

Rabies virus variants isolated from humans or other mammalian species can be identified by reverse-transcription polymerase chain reaction (RT-PCR) amplification and sequencing or by characterization with monoclonal antibodies. These techniques are helpful in human cases with no known history of exposure. Worldwide, most human rabies is transmitted from dogs in countries with endemic canine rabies and dog-to-dog transmission, and human cases can be imported by travelers returning from these regions. In North America, human disease is usually associated with transmission from bats; there may be no known history of bat bite or other bat exposure in these cases. Most human cases are due to a bat rabies virus variant associated with silver-haired and tricolored bats. These are small bats whose bite may not be recognized, and the virus has adapted for replication at skin temperature and in cell types that are present in the skin.

Transmission from nonbite exposures is relatively uncommon. Aerosols generated in the laboratory or in caves containing millions of Brazilian free-tail bats have rarely caused human rabies. Transmission has resulted from corneal transplantation and also from solid organ transplantation and a vascular conduit (for a liver transplant) from undiagnosed donors with rabies in Texas, Florida, and Germany. Human-to-human transmission is extremely rare, although hypothetical concern about transmission to health care workers has prompted the implementation of barrier techniques to prevent exposures.

PATHOGENESIS

The incubation period of rabies (defined as the interval between exposure and the onset of clinical disease) is usually 20–90 days but in rare cases is as short as a few days or >1 year. During most of the incubation period, rabies virus is thought to be present at or close to the site of inoculation (Fig. 232-2). In muscles, the virus is known to bind to nicotinic acetylcholine receptors on postsynaptic membranes at neuromuscular junctions, but the exact details of viral entry into the skin and SC tissues have not yet been clarified. Rabies virus spreads centripetally along peripheral nerves toward the CNS at a rate of up to ~250 mm/d via retrograde fast axonal transport to the spinal cord or brainstem. Once the virus enters the CNS, it rapidly disseminates to other regions of the CNS via fast axonal transport along neuroanatomic connections. Neurons are prominently infected in rabies; infection of astrocytes is unusual. After CNS infection becomes established, there is centrifugal spread along sensory and autonomic nerves to other tissues, including the salivary glands, heart, adrenal glands, and skin. Rabies virus replicates in acinar cells of the salivary glands and is secreted in the saliva of rabid animals that serve as vectors of

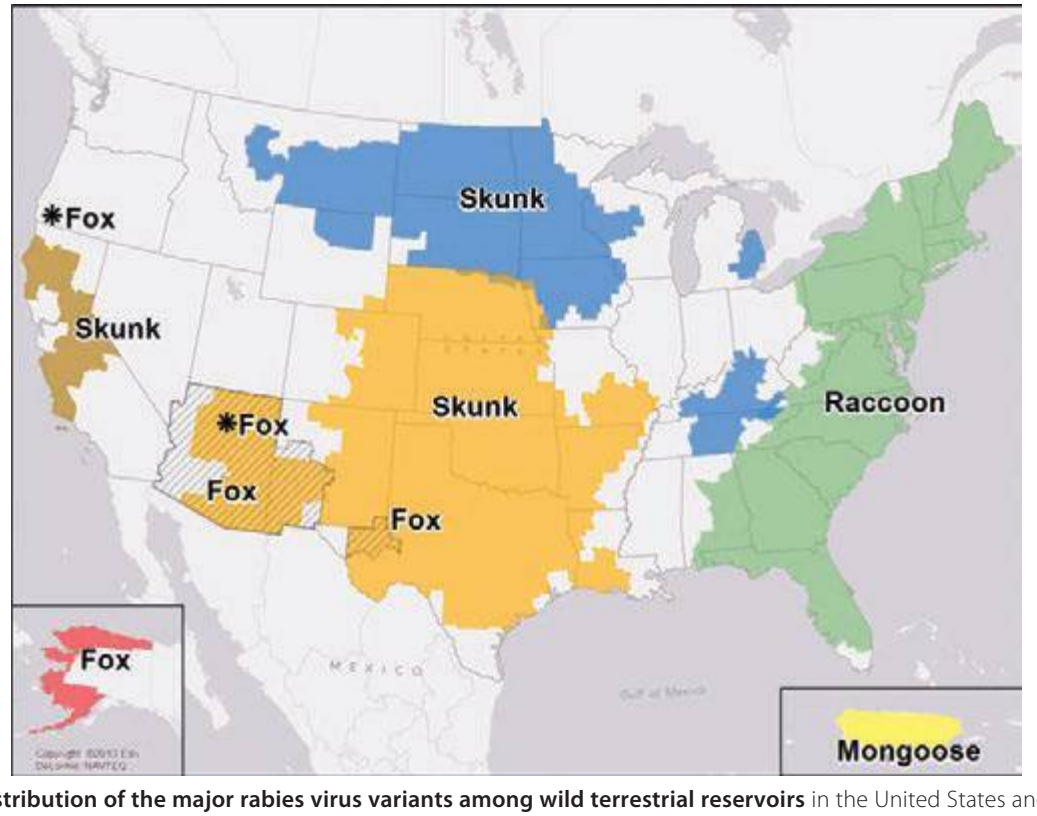

FIGURE 232-1 Distribution of the major rabies virus variants among wild terrestrial reservoirs in the United States and Puerto Rico, 2008–2012. *Potential host-shift event. *(From JL Dyer et al: J Am Vet Med Assoc 243:805, 2013.)*