Mumps virus also can spread to other sites, including the CNS, testis, ovary, and pancreas. Aseptic meningitis is the most common extrasalivary gland complication of mumps infection, occurring in up to 15% of cases. The mumps vaccine has reduced the incidence of mumps by 99% in the United States. The diagnosis is usually made clinically, but serology, viral culture, or PCR assays can be used for definitive diagnosis.

MORPHOLOGY

Mumps parotitis is bilateral in 70% of cases. The affected glands are enlarged, have a doughy consistency, and are moist, glistening, and reddish-brown on cross-section. On microscopic examination the gland interstitium is edematous and diffusely infiltrated by macrophages, lymphocytes, and plasma cells, which compress acini and ducts. Neutrophils and necrotic debris may fill the duct lumen and cause focal damage to the lining epithelium.

In **mumps orchitis** testicular swelling may be marked, caused by edema, mononuclear cell infiltration, and focal hemorrhages. Because the testis is tightly contained within the tunica albuginea, parenchymal swelling may compromise the blood supply and cause areas of infarction. The testicular damage can lead to scarring, atrophy, and, if severe, sterility.

Infection and damage of acinar cells in the **pancreas** may release digestive enyzmes, causing parenchymal and fat necrosis and neutrophil-rich inflammation. **Mumps encephalitis** causes perivenous demyelination and perivascular mononuclear cuffing.

Poliovirus Infection

Poliovirus causes an acute systemic viral infection, leading to a wide range of manifestations, from mild, self-limited infections to paralysis of limb muscles and respiratory muscles. Poliovirus is a spherical, unencapsulated RNA virus of the enterovirus genus. Other enteroviruses cause childhood diarrhea as well as rashes (coxsackievirus A), conjunctivitis (enterovirus 70), viral meningitis (coxsackieviruses and echovirus), and myopericarditis (coxsackievirus B). There are three serotypes of poliovirus, each of which is included in the Salk formalin-fixed (killed) vaccine and the Sabin oral, attenuated (live) vaccine. These vaccines have nearly eradicated polio, because the poliovirus infects only humans, shows limited genetic variation, and is effectively neutralized by antibodies generated by immunization. Nevertheless, this scourge persists in parts of the developing world, particularly in areas of political unrest and war. According to global polio surveillance data, in 2013, a total of 328 polio cases were reported from Afghanistan, Cameroon, Ethiopia, Kenya, Nigeria, Pakistan, Somalia, and Syria.

Poliovirus, like other enteroviruses, is transmitted by the fecal-oral route. The virus infects human cells by binding to CD155, an epithelial adhesion molecule. The virus is ingested and replicates in the mucosa of the pharynx and gut, including tonsils and Peyer patches in the ileum. Poliovirus then spreads through lymphatics to lymph nodes and eventually the blood, producing transient viremia and fever. Although most poliovirus infections are asymptomatic, in about 1 of 100 infected persons poliovirus invades the CNS and replicates in motor neurons of the spinal cord (spinal poliomyelitis) or brain stem (bulbar poliomyelitis). Antiviral antibodies control the disease in most cases; it is not known why they fail to contain the virus in some individuals. Viral spread to the nervous system may be through the blood or by retrograde transport of the virus along axons of motor neurons. Rare cases of poliomyelitis that occur after vaccination are caused by mutations of the attenuated viruses to wild-type forms. The diagnosis can be made by viral culture or PCR of throat secretions or stool, or by serology. The neurologic features and neuropathology of poliovirus infection are described in Chapter 28.

West Nile Virus

West Nile Virus is an acute systemic viral infection that causes a mild, self-limited infection or neuroinvasive disease associated with long-term neurologic sequelae. West Nile virus is an arthropod-borne virus (arbovirus) of the flavivirus group, which also includes viruses that cause dengue fever and yellow fever. West Nile virus has a broad geographic distribution in the Old World, including Africa, the Middle East, Europe, Southeast Asia, and Australia. It was first detected in the United States in 1999 during an outbreak in New York City, and has since spread across the United States; in the year 2013, a least one case was reported in 44 states. West Nile virus is transmitted by mosquitoes to birds and to mammals. Infected birds develop prolonged viremia and are the major reservoir for the virus. Humans are incidental hosts. Most affected patients acquire the infection from a mosquito bite; less commonly, human-to-human transmission occurs by blood transfusion, organ transplantation, breast-feeding, or transplacental spread.

After inoculation by a mosquito, West Nile virus replicates in skin dendritic cells, which then migrate to lymph nodes. Here, the virus replicates further, enters the bloodstream, and, in some individuals, crosses the blood-brain barrier. In the CNS, the virus infects neurons. Chemokines have critical roles in recruiting leukocytes to the CNS, where they assist in viral clearance. The chemokine receptor CCR5 contributes to resistance to neuroinvasive infection, hence mutations in both copies of the CCR5 gene that lead to loss of function are associated with an increased rate of symptomatic infection. Recall that in HIV infection the role of this receptor is the opposite—CCR5 loss-of-function is protective because HIV uses the receptor to infect host T cells (Chapter 6).

West Nile virus infection is usually asymptomatic, but in 20% of infected individuals it gives rise to a fever, headache, myalgia, fatigue, anorexia, and nausea. A maculopapular rash is seen in approximately half the cases. CNS complications (meningitis, encephalitis, meningoencephalitis) occur in about 1 in 150 clinically apparent infections. Meningoencephalitis has a mortality of about 10% and results in long-term cognitive and neurologic impairment in many survivors. Perivascular and leptomeningeal chronic inflammation, microglial nodules (Chapter 28), and neuronophagia predominantly involving the temporal lobes and brain stem have been observed in patients who died of West Nile virus infection. Immunosuppressed persons and older adults appear to be at the greatest risk for severe disease. Rare complications include hepatitis, myocarditis, and pancreatitis. The diagnosis is usually