new genetic variants arise periodically in nature. Immunity to some viruses wanes with time, and this too may allow the same virus to infect the host repeatedly (e.g., respiratory syncytial virus).

Measles

Measles is an acute viral infection that affects multiple organs and causes a wide range of disease, from mild, self-limited infections to severe systemic manifestations. Measles (rubeola) virus is a leading cause of vaccine-preventable death and illness worldwide. More than 20 million people acquire measles each year. In 2010, measles accounted for an estimated 139,000 deaths globally, the majority in children in developing countries. Because of poor nutrition and lack of access to medical care, children in developing countries are 10 to 1000 times more likely to die of measles than are children in developed countries. Measles can produce severe disease in people with defects in cellular immunity (e.g., people infected with HIV or people with a hematologic malignancy). Epidemics of measles occur among unvaccinated individuals. In the United States, the incidence of measles has decreased dramatically since 1963, when a measles vaccine was licensed, and endemic transmission was eliminated in 2000. The diagnosis may be made clinically, by serology, or by detection of viral antigen in nasal exudates or urinary sediments.

Pathogenesis. Measles virus is a single-stranded RNA virus of the paramyxovirus family, which includes mumps, respiratory syncytial virus, parainfluenza virus (a cause of croup), and human metapneumovirus. There is only one serotype of measles virus. Measles virus is transmitted by respiratory droplets. Three cell-surface receptors have been identified for the virus: CD46 (a complement-regulatory protein that inactivates C3 convertases), signaling lymphocytic activation molecule (SLAM, a molecule involved in T-cell activation), and nectin 4 (adherens junction protein). CD46 is expressed on all nucleated cells, while SLAM is expressed on cells of the immune system, and nectin 4 is expressed on epithelial cells. All of these receptors bind the viral hemagglutinin protein.

Measles can replicate in a variety of cell types, including epithelial cells and leukocytes. The virus initially multiplies within the respiratory tract and then spreads to local lymphoid tissues. Replication of the virus in lymphatic tissue is followed by viremia and systemic dissemination to many tissues, including the conjunctiva, skin, respiratory tract, urinary tract, small blood vessels, lymphatic system, and CNS. Most children develop T-cell–mediated immunity to measles virus that helps control the viral infection and produces the measles rash. Hence, the rash is less frequent in people with deficiencies in cell-mediated immunity. In addition, in malnourished children with poor medical care, measles virus may cause croup, pneumonia, diarrhea and protein-losing enteropathy, keratitis leading to scarring and blindness, encephalitis, and hemorrhagic rashes ("black measles").

Antibody-mediated immunity to measles virus protects against reinfection. Measles also can cause transient but profound immunosuppression, resulting in secondary bacterial and viral infections, which are responsible for much of measles-related morbidity and mortality. Alterations of both innate and adaptive immune responses occur following measles infection, including defects in dendritic cell and lymphocyte function. Subacute sclerosing panencephalitis (Chapter 28) and measles inclusion body encephalitis (in immunocompromised individuals) are rare late complications of measles. The pathogenesis of subacute sclerosing panencephalitis is not well understood, but a replication-defective variant of measles may be involved in this persistent viral infection.

MORPHOLOGY

The blotchy, reddish brown rash of measles virus infection on the face, trunk, and proximal extremities is produced by dilated skin vessels, edema, and a mononuclear perivascular infiltrate. Ulcerated mucosal lesions in the oral cavity near the opening of the Stensen ducts (the pathognomonic **Koplik spots**) are marked by necrosis, neutrophilic exudate, and neovascularization. The lymphoid organs typically have marked follicular hyperplasia, large germinal centers, and randomly distributed multinucleate giant cells, called **Warthin-Finkeldey cells**, which have eosinophilic nuclear and cytoplasmic inclusion bodies. These are pathognomonic of measles and are also found in the lung and sputum (Fig. 8-8). The milder forms of measles pneumonia show the same peribronchial and interstitial mononuclear cell infiltration that is seen in other nonlethal viral infections.

Mumps

Mumps is an acute systemic viral infection usually associated with pain and swelling of the salivary glands. Like measles virus, mumps virus is a member of the paramyxovirus family. Mumps virus has two types of surface glycoproteins, one with hemagglutinin and neuraminidase activities and the other with cell fusion and cytolytic activities. Mumps viruses enter the upper respiratory tract through inhalation of respiratory droplets, spread to draining lymph nodes where they replicate in lymphocytes (preferentially in activated T cells), and then spread through the blood to the salivary and other glands. Mumps virus infects salivary gland ductal epithelial cells, resulting in desquamation of involved cells, edema, and inflammation that leads to the classic salivary gland pain and swelling.

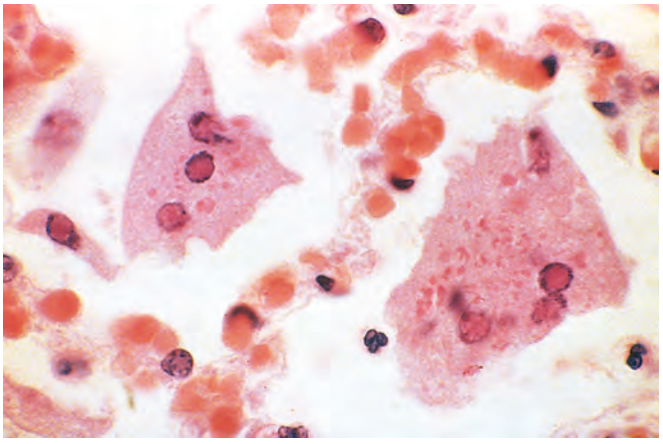

Figure 8-8 Measles giant cells in the lung. Note the glassy eosinophilic intranuclear inclusions.