a continuous supply of susceptible individuals. Newborns become susceptible to measles virus infection when passively acquired maternal antibody is lost; when not vaccinated, these infants account for the bulk of new susceptible individuals.

Endemic measles has a typical temporal pattern characterized by yearly seasonal epidemics superimposed on longer epidemic cycles of 2–5 years or more. In temperate climates, annual measles outbreaks typically occur in the late winter and early spring. These annual outbreaks are probably attributable to social networks facilitating transmission (e.g., congregation of children at school) and environmental factors favoring the viability and transmission of measles virus. Measles cases continue to occur during interepidemic periods in large populations, but at low incidence. The longer epidemic cycles occurring every several years result from the accumulation of susceptible persons over successive birth cohorts and the subsequent decline in the number of susceptibles following an outbreak.

Secondary attack rates among susceptible household and institutional contacts generally exceed 90%. The average age at which measles occurs depends on rates of contact with infected persons, protective maternal antibody decline, and vaccine coverage. In densely populated urban settings with low-level vaccination coverage, measles is a disease of infants and young children. The cumulative distribution can reach 50% by 1 year of age, with a significant proportion of children acquiring measles before 9 months—the age of routine vaccination in many countries, in line with the schedule recommended by the WHO's Expanded Programme on Immunization. As measles vaccine coverage increases or population density decreases, the age distribution shifts toward older children. In such situations, measles cases predominate in school-age children. Infants and young children, although susceptible if not protected by vaccination, are not exposed to measles virus at a rate sufficient to cause a large disease burden in this age group. As vaccination coverage increases further, the age distribution of cases may be shifted into adolescence and adulthood; this distribution is seen in measles outbreaks in the United States and necessitates targeted measles vaccination programs for these older age groups.

Persons with measles are infectious for several days before and after the onset of rash, when levels of measles virus in blood and body fluids are highest and when cough, coryza, and sneezing, which facilitate virus spread, are most severe. The contagiousness of measles before the onset of recognizable disease hinders the effectiveness of quarantine measures. Viral shedding by children with impaired cell-mediated immunity can be prolonged.

Medical settings are well-recognized sites of measles virus transmission. Children may present to health care facilities during the prodrome, when the diagnosis is not obvious although the child is infectious and is likely to infect susceptible contacts. Health care workers can acquire measles from infected children and transmit measles virus to others. Nosocomial transmission can be reduced by maintenance of a high index of clinical suspicion, use of appropriate isolation precautions when measles is suspected, administration of measles vaccine to susceptible children and health care workers, and documentation of health care workers' immunity to measles (i.e., proof of receipt of two doses of measles vaccine or detection of antibodies to measles virus).

As efforts at measles control are increasingly successful, public perceptions of the risk of measles as a disease diminish and are replaced by concerns about possible adverse events associated with measles vaccine. As a consequence, numerous measles outbreaks have occurred because of opposition to vaccination on religious or philosophical grounds or unfounded fears of serious adverse events (see "Active Immunization," below).

PATHOGENESIS

Measles virus is transmitted primarily by respiratory droplets over short distances and, less commonly, by small-particle aerosols that remain suspended in the air for long periods. Airborne transmission appears to be important in certain settings, including schools, physicians' offices, hospitals, and enclosed public places. The virus can be transmitted by direct contact with infected secretions but does not survive for long on fomites.

The incubation period for measles is ~10 days to fever onset and 14 days to rash onset. This period may be shorter in infants and longer (up to 3 weeks) in adults. Infection is initiated when measles virus is deposited on epithelial cells in the respiratory tract, oropharynx, or conjunctivae (Fig. 229-1*A*). During the first 2–4 days after infection, measles virus proliferates locally in the respiratory mucosa and spreads to draining lymph nodes. Virus then enters the bloodstream in infected leukocytes (primarily monocytes), producing the primary viremia that disseminates infection throughout the reticuloendothelial system. Further replication results in secondary viremia that begins 5–7 days after infection and disseminates measles virus throughout the body. Replication of measles virus in these target organs, together with the host's immune response, is responsible for the signs and symptoms of measles that occur 8–12 days after infection and mark the end of the incubation period (Fig. 229-1*B*).

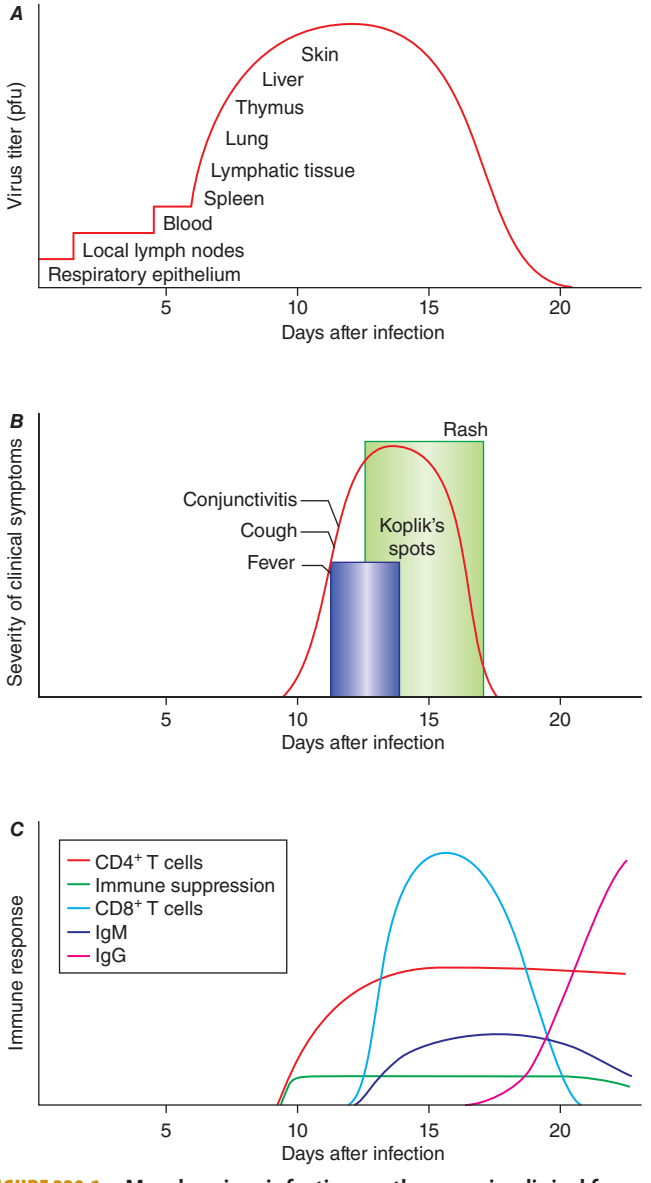

FIGURE 229-1 Measles virus infection: pathogenesis, clinical features, and immune responses. ***A.*** Spread of measles virus, from initial infection of the respiratory tract through dissemination to the skin. ***B.*** Appearance of clinical signs and symptoms, including Koplik's spots and rash. ***C.*** Antibody and T cell responses to measles virus. The signs and symptoms of measles arise coincident with the host immune response. *(Source: Modified from WJ Moss, DE Griffin: Nat Rev Microbiol 4:900, 2006.)*