areas of transmission (mostly in Miami, Florida) and travel advisories issued by the CDC. Internationally, efforts are actively under way to develop a vaccine against Zika virus. Considering that Zika virus is now endemic in about 75 different countries, development of an effective vaccine seems to be the most promising way to deal with this problem. Currently, a number of Phase I clinical trials are underway to develop a safe and effective vaccine against Zika virus disease. In January 2018, the U.S. Food and Drug Administration granted a fast track designation to Takeda Pharmaceutical company's Zika vaccine candidate TAK-429. On July 5, 2018, the FDA also approved the Procleix Zika Virus Assay developed by Grifols Diagnostic Solutions Inc. to detect Zika virus RNA in plasma.

7.11 Ebola Virus Outbreak: West Africa 2014

Ebola virus disease, formerly knowns as Ebola hemorrhagic fever, a relatively rare but frequently fatal disease in humans and other primates, is caused in humans by four of the five strains of the *Ebolavirus* genus of the family Filoviridae. These strains are found in several African countries. The virus was first identified in 1976 near the Ebola River in the Democratic Republic of the Congo.[33] The natural reservoir of the virus is not definitively known, but it is believed to have an animal host, most likely bats. How the virus transfers from the animal host to humans is not understood, but the disease spreads among humans through direct contact (skin, eye, or oronasal mucuous membranes) with the blood or bodily fluids (saliva, sweat, semen, breast milk, vomit, urine, or feces) of a person with EVD, objects such as needles and syringes contaminated with the bodily fluids of an EVD patient, or contact with bats and nonhuman primates (monkeys and apes). Sexual contact with a person with the virus is also a mode of transmission of EVD. Transmission during outbreaks commonly occurs through contact with family members, caregivers, and funeral preparations and ceremonies. The clinical presentation of the diseases includes fever, vomiting, severe headache, fatigue, malaise, abdominal pain, diarrhea, and unexplained bleeding. Patients who survive EVD develop antibodies that last for 10 or more years.[33]

In the last two decades, there have been several outbreaks of EVD in various African countries, including Uganda, Gabon, Sudan, and Congo.[14,15,33] The largest and most recent outbreak started in Guinea in early 2014 and quickly spread to Liberia and Sierra Leone. It took a concerted international effort under the United Nations Mission for Ebola Emergency Response to bring this outbreak under control by the spring of 2015, although sporadic cases continued to be reported from Liberia, Sierra Leone, and Guinea until September 2015.[14,15] It was only on January 14, 2016, that the World Health Organization declared all three of these countries to be free of Ebola transmission. Altogether, this outbreak resulted in 28,616 cases of Ebola in these three West African countries, with 15,227 laboratory-confirmed cases and 11,310 deaths. Additionally, 36 travel-related Ebola cases were reported in seven other countries (Italy, Mali, Nigeria, Senegal, Spain, the United Kingdom, and the United States), with 34 laboratory-confirmed diagnoses and 15 deaths.[14,15]

A combined phase II and phase III unblinded vaccine trial is currently under way in Sierra Leone in collaboration with the CDC to assess the safety and efficacy of a vaccine called the rVSV-ZEBOV candidate Ebola vaccine.[34] The trial, named Sierra Leone Trial to Introduce a Vaccine (STRIVE), involves 8,650 adult healthcare and other frontline workers, including doctors, nurses, ambulance teams, laboratory technicians, pharmacy workers, and burial workers. The participants were randomly divided into *vaccination* (immediate) and *defferred vaccination* groups. No placebo was given to any participants in this trial. The vaccination group was given the vaccine within 1 week of enrollment, whereas the defferred vaccination group was given the vaccine 6 months later. The follow-up period was 6 months. The first 400 participants were enrolled in a substudy involving more frequent follow-up to detect adverse events such as fever, rash, and headache. The participants were asked to keep a diary of events and were followed through scheduled monthly phone calls. An immunogenicity substudy with 500 participants is also being conducted to assess the immune response to the vaccine. The vaccine being used in STRIVE is a recombinant vesicular stomatitis virus, *Zaire ebolavirus vaccine*, which was developed in Canada. It contains a weakened vesicular stomatitis virus in which a single gene of the virus is replaced with a single ebolavirus gene. Because the whole ebolavirus is not used, the vaccine cannot cause EVD. Other studies with the same vaccine have been conducted and are continuing in Gabon, Kenya, Germany, Canada, and the United States. Similar phase II and phase III trials are being conducted in Liberia and and Guinea.

CASE STUDY 7.1: California Measles Outbreak 2014

Modified from: Zipprich J, Winter K, Hacker J, Xia D, Watt J, Harriman K. Measles outbreak – California, December 2014–February 2015. Morbid Mortal Wkly Rep. 2015;64(6):153–154. Accessed July 3, 2017. https://www.cdc.gov/mmwr/pdf/wk/mm6406.pdf

A suspected case of measles—an 11-year-old unvaccinated hospitalized child with a rash that started on December 28, 2014—was reported to the California Department of Public Health (CDPH) on January 5, 2015. The only notable part of the history was a visit to one of the two adjacent Disney theme parks in Orange County, California. On the same date, CDPH was notified of six other suspected cases of measles; four were California residents and two were Utah residents. All six had visited one or both Disney theme parks during the period December 17–20, 2014. By January 7, 2015, there were seven confirmed cases in California. By February 11, a total of 125 confirmed U.S. resident cases (110 California residents and 15 in seven other states) linked to this outbreak with rash onset between December 28, 2014 and February 8, 2015 had been reported. Additionally, 11 linked cases were reported from Mexico (1) and Canada (10). Out of the 110 California resident cases, 39 (35%) had visited one or both of the theme parks during December 17–20, 2014. Of the remaining 71 California cases, 34 were secondary cases (mostly household or close contacts), while source of exposure for 37 was unknown. Among the 110 California cases, 49 (45%) were unvaccinated, 47 (43%) had unknown vaccination status, and 14 were partially (12) or completely (1) vaccinated or had immunoglobuline G seropositivity (1). Among the 49 unvaccinated cases, 12 were too young to be vaccinated and 28 were intentionally unvaccinated because of personal beliefs. The age range for cases was 6 weeks to 70 years. The two Disney theme parks in California have approximately 24 million visits every year, with many international visitors from measles-endemic countries.

FIGURE 7.10 shows the epidemic curve for this outbreak.

Questions

Question 1. What was the approximate length of the incubation period? Explain your ansewer with the help of data from the outbreak and Figure 7.10.

Question 2. Was this a point source, common source, or mixed propagated outbreak? Explain your answer with the help of data from the outbreak.

Question 3. When did the peak of the outbreak occur? Explain your answer with the help of data from the outbreak and Figure 7.10.

Question 4. Did the outbreak end spontaneously, or did it end because of control measures implemented by the local health authorities? Explain your answer with the help of data from the outbreak.

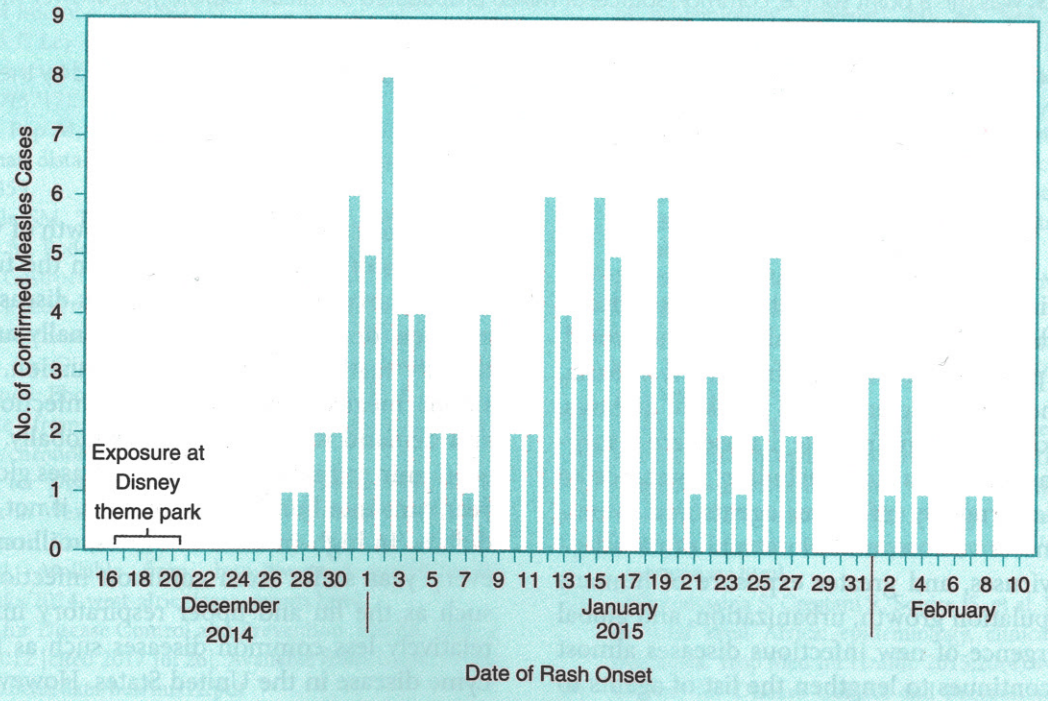

FIGURE 7.10 Number of confirmed measles cases (N = 110)* by date of rash onset, California, December 2014–February 2015.

*Reported to California Department of Health as of February 11, 2015.

Reproduced from: Zipprich J, Winter K, Hacker J, Xia D, Watt J, Harriman K. Measles outbreak – California, December 2014–February 2015. Morbid Mortal Wkly Rep. 2015;64(6):153–154. Accessed July 3, 2017. https://www.cdc.gov/mmwr/pdf/wk/mm6406.pdf