US Presidential Executive Order 13295 designates eight infectious conditions as candidates for federally imposed quarantine. Five of these conditions are already covered in chapters 10–14 of this manual. Here we address the remaining diseases: cholera, diphtheria, and yellow fever.

**Cholera**

Cholera, caused by the gram-negative bacterium *Vibrio cholerae*, is characterized by profuse watery diarrhea. The volume of stool output among cholera victims can be so great that voluntary oral fluid intake is inadequate to keep up with losses. In the absence of ongoing fluid replacement with intravenous fluids or oral rehydration solutions, patients can succumb to dehydration and electrolyte imbalances. Although the average infectious dose of ~100 million organisms is high in comparison to many other infectious diseases described in this manual, one gram of stool from a person infected with cholera may contain trillions of organisms, thus enhancing the potential for disease spread. Cholera is typically acquired as a result of poor environmental hygiene and consumption of feces-contaminated water, rather than direct person-to-person transmission. The vast majority of cholera cases occur in resource-poor areas of sub-Saharan Africa and in the Ganges.
River delta of Bangladesh and eastern India, where fecal matter often contaminates drinking water sources.

**Isolation.** Transmission in health care settings is rare and can be avoided by simple handwashing and meticulous attention to the proper handling of human waste and contaminated linens. For these reasons, cholera patients would not likely require high-level isolation in an inpatient setting.

**Quarantine.** The quarantine of asymptomatic individuals in order to stop a cholera outbreak would also be unnecessary in most instances. While experience in the 19th century, when ships were quarantined in New York’s East River near Bellevue Hospital, attests to the effectiveness of such measures, the utility of simpler methods to reduce disease spread, such as those taken by John Snow (who legend has it halted a cholera outbreak in London by removing a water pump handle), argue against its necessity in most cases. Nonetheless, cholera remains subject to federal quarantine in the United States and had long been one of the World Health Organization’s (WHO) few quarantinable diseases. It is thus conceivable that quarantine might be employed as an adjunct to other hygiene-based control measures should a cholera outbreak occur. As humans are the only reservoir of cholera (although the causative organism survives *ex vivo* in salt water), the disease presents an eradication target. Future efforts aimed at mopping up remaining pockets of disease might include human quarantine. The short incubation period of cholera (2 hours to 5 days) means that such quarantine would likely be limited in duration but also challenging to implement effectively in a rapidly expanding outbreak.

Finally, vaccination might be offered to health care workers and close contacts of cholera victims as an adjunct to hygiene-based measures. Vaxchora®, licensed in the United States in 2016, offers short-term protection against *V. cholera* strain O1 (the historical cause of cholera in Africa and Asia) to a majority of recipients. It does not protect against other cholera strains, including *V. cholera* strain O139, found in the Americas.
Diphtheria

Diphtheria, caused by the gram-positive bacillus *Corynebacterium diphtheriae*, most often presents as a severe pharyngeal or laryngeal infection. Victims risk airway obstruction and hypoxia caused by edema and necrosed infected tissues in the posterior pharynx known as pseudomembranes. A potent toxin produced by the organism can also cause fatal myocarditis and other complications. Cutaneous infection can occasionally occur. Diphtheria is generally transmitted person to person through direct contact with nasopharyngeal secretions or droplets. The incubation period is 1–10 days. In colonial times, diphtheria was a major cause of childhood mortality. The appearance of diphtheria, which is extremely contagious via respiratory droplets, in a village could threaten its entire pediatric population. Extraordinarily effective vaccines against the toxin, available since 1921, as well as antibiotics, have nearly eliminated diphtheria from most developed nations. Its propensity for a rapid return, however, is illustrated by outbreaks that occurred in the 1990s in all 15 republics of the former Soviet Union following the dissolution of the latter and a consequent breakdown in public health infrastructure and immunization efforts.

**Isolation.** The institution of droplet precautions would constitute adequate isolation for a hospitalized patient with diphtheria.

**Quarantine.** While quarantine was a mainstay of diphtheria control in the pre-antibiotic era, it would not likely be necessary in most cases today, although short-term confinement of close contacts of diphtheria patients might be utilized to facilitate administration of prophylactic antitoxin. It is also conceivable that public health authorities might, in the face of a diphtheria outbreak, invoke quarantine in the management of unvaccinated individuals, vaccine refusers, other noncompliant persons, and potential super-spreaders. Like cholera, diphtheria has no animal reservoir and presents an eradication target. Limited quarantine might have a role in such efforts in the future.
Yellow Fever

Yellow fever is a disease of humans and other primates and is caused by a flavivirus transmitted by *Aedes* mosquitoes. In roughly 85% of patients, the illness is self-limited and presents, following a 3–6 day incubation period, with headache and high fever. While these symptoms typically resolve within a few days, a secondary phase occurs in a minority of patients. This phase involves gastrointestinal signs and symptoms (vomiting, epigastric pain, and jaundice) as well as a bleeding diathesis, manifest by hematemesis, melena, hematuria, ecchymoses, and other signs of clotting dysfunction and hemorrhage. The scleral icterus often seen at this point lends the disease its name, and renal insufficiency as well as cardiovascular instability are common in this later stage. Viremia is usually present only during the first three days of illness, and while the disease is not directly transmissible from person to person, viremic patients risk infecting local mosquitoes.

**Isolation.** Because the disease is not generally transmissible except via these arthropod vectors, standard precautions are adequate in managing hospitalized patients. A licensed vaccine, YF-Vax®, is offered to (and sometimes required of) persons in the United States traveling to endemic areas. Various other yellow fever vaccines are available in a number of foreign countries, although shortages of vaccine have hampered immunization efforts. Because of the lack of person-to-person transmission, vaccines would likely be of little benefit to health care workers in nonendemic areas.

**Quarantine.** *Aedes* mosquitoes are found throughout the tropics, the subtropics, and in many parts of the temperate world; therefore, concern for reintroducing yellow fever to geographic areas from which it had been eliminated might prompt quarantine of a patient.

**Other Diseases**

In the past, quarantine has been used for patients feared to be harboring polio, typhoid fever, typhus, anthrax, leprosy, and scarlet fever. None of these diseases remain on current lists of quarantinable conditions and all can be controlled by far less restrictive means. Typhus and anthrax
are not transmitted from person-to-person, while polio and typhoid are contagious only via the fecal-oral route. Leprosy has nearly been eliminated from the developed world and is only minimally communicable. Scarlet fever has become a relatively trivial disease in the antibiotic era. Nonetheless, as humanity enters the final stages of polio eradication and leprosy elimination, it remains possible that quarantine could be ordered in isolated circumstances (to vaccine refusers, in the case of polio, for instance). Conversely, as old diseases are eradicated, new ones will continue to emerge. Consequently, the list of diseases subject to quarantine will likely evolve further over time.